Journal of Cardiology 64 (2014) 19–24

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Evaluation of hemodynamically severe coronary stenosis as determined by fractional flow reserve with frequency domain optical coherence tomography measured anatomical parameters

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ARTICLE INFO

Article history:
Received 31 July 2013
Received in revised form 9 October 2013
Accepted 7 November 2013
Available online 22 December 2013

Keywords:
Frequency domain optical coherence tomography
Fractional flow reserve
Coronary stenosis
Minimal lumen area
Minimal lumen diameter

ABSTRACT

Objectives: The main objective of this study is to determine the correlation between fractional flow reserve (FFR)- and frequency domain optical coherence tomography (FD-OCT)-measured lumen parameters, and to determine the diagnostic competence of FD-OCT concerning the identification of severe coronary stenosis.
Methods: A total of 41 coronary stenoses in 30 patients were assessed consecutively by quantitative coronary angiography (QCA), FFR, and FD-OCT. Stenoses were labeled severe if FFR $\leq$ 0.80. The minimal lumen area (MLA), minimal lumen diameter (MLD), and percent lumen area stenosis (%AS) were measured using FD-OCT.
Results: FFR was $\leq$0.80 in 10 stenoses (24.4%). A poor but significant correlation between FFR and FD-OCT-measured MLA ($r^2 = 0.4$, $p < 0.001$), MLD ($r^2 = 0.28$, $p < 0.001$), and %AS ($r^2 = 0.13$, $p = 0.02$) was found. In the overall group, the diagnostic efficiency of MLA and MLD in identifying significant stenosis was moderate. The area under the curve (AUC) was 0.80 [95% confidence interval (CI): 0.64–0.91] for MLA and 0.76 (95% CI: 0.60–0.88) for MLD. The best cut-off values of FD-OCT-measured lumen parameters to identify stenosis with FFR $\leq$ 0.80 were 1.62 mm^2 [specificity 97%, sensitivity 70%, positive predictive value (PPV) 89% and negative predictive value (NPV) 91%] for MLA and 1.23 mm (specificity 87%, sensitivity 70%, PPV 64% and NPV 90%) for MLD. The diagnostic efficiency of MLA in identifying significant stenosis in vessels having reference diameter < 3 mm was high. The AUC was 0.96 (95% CI: 0.83–1.0).
Conclusions: The FFR values and FD-OCT anatomical parameters MLA, MLD were found to be significantly correlated. In the overall group, the FD-OCT-measured MLA and MLD have shown moderate diagnostic efficiency in the functional evaluation of significant stenosis. FD-OCT-measured MLA has high diagnostic efficiency in identifying severe coronary stenosis in vessels having reference diameter <3 mm.

Introduction

The revascularization of intermediate coronary lesions, having stenosis diameter of 40–70% on angiography, involves detailed characterization to answer the associated anatomic and physiologic issues. Quantitative coronary angiography (QCA) has advanced to provide more accurate measurements related to coronary vascular tree and complex lesions, but the un-incorporated parameters such as length, entrance angle, coefficient of separation of laminar flow in QCA, the assessment of intermediate coronary stenosis via angiogram, or QCA are inaccurate [1]. Therefore additional diagnostic methods are used to determine the clinical impact of such stenosis. The fractional flow reserve (FFR) technique, which measures pressure gradient across an artery stenosis, is considered as

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http://dx.doi.org/10.1016/j.jjcc.2013.11.009

a gold standard in the evaluation of the severity of such stenosis. The FFR value ≤0.8 is considered clinically important and is treated as an indication of severe stenosis [2–6]. Intravascular ultrasound (IVUS) is a catheter-based invasive imaging technique used for anatomic and morphological assessment of lesions and is capable of providing information about lumen area, vessel area, and plaque burden. Several studies have investigated the use of IVUS in the identification of severe stenosis using FFR as a standard tool [7–13]. Intra coronary optical coherence tomography (OCT) is a new imaging technique which is analogous to IVUS, but uses near-infrared light rather than sound waves. OCT provides high-resolution (10 times higher than IVUS), cross-sectional tomographic images of coronary arteries and deployed stents [14]. The higher spatial resolution of OCT as compared to IVUS provides better details of the luminal-intima boundary and allows lumen area measurements with excellent reproducibility [15–19]. The time domain OCT (TD-OCT) systems have a lower pullback speed (1–3 mm/s) and a frame rate (15–20 frames/s), while frequency domain (FD)-OCT systems have higher pullback speed up to 20 mm/s and a frame rate of 100 frames/s [20]. Because of these features FD-OCT systems are now being widely used in modern catheterization laboratories globally. The main objective of this study is to determine the correlation between FFR- and FD-OCT-measured anatomical parameters that include minimal lumen area (MLA), minimal lumen diameter (MLD), and percent lumen area stenosis (%AS). The diagnostic efficiency of FD-OCT in identifying severe coronary stenosis as determined by FFR is also included.

Materials and methods

A total of 41 coronary stenoses were examined in 30 patients scheduled for coronary angiography due to stable angina and/or ischemia documented on exercise stress test at University Hospital Galway (UHS), Ireland between October 2011 and May 2013. FFR measurement, FD-OCT, and QCA analysis were performed in all patients. They all had at least 1 target vessel with stenosis (>30% diameter stenosis by visual estimation). Serial stenosis, left main stenosis, stenosis located in culprit vessels of acute coronary syndromes, bypass graft stenosis, and anatomical characteristics that limited the advancement of OCT catheter were excluded from the study. The study was approved by Galway clinical research ethics committee and informed consent was obtained from the patients.

Angiographic views were acquired after intracoronary nitrates (0.1 mg). The QCA analysis (percent diameter stenosis and percent area stenosis) was performed using validated QCA software (CASS II, Pie Medical Imaging, BV, Maastricht, The Netherlands) separately blinded to the results of OCT and FFR.

A coronary pressure wire (St. Jude Medical, St. Paul, MN, USA) was employed to measure FFR. Measurements were obtained at maximum hyperemia induced by intravenous adenosine, managed at 140 μg/kg/min through a large peripheral vein. FFR was calculated as the ratio of the intracoronary pressure to the aortic pressure during hyperemia. Stenoses were labeled severe if FFR ≤ 0.80.

The OCT imaging of the target stenosis was performed using a commercial FD OCT system (C7XR) and the Dragonfly catheter (Lightlab Imaging Inc., Westford, MA, USA). This system uses a swept source laser with central wavelength of 1300 nm which provides an axial resolution of 10–15 μm and gives tissue penetration of 1–3 mm. The system has a lateral resolution of 25 μm. The pullback speed of 20 mm/s was used and blood clearance was performed by injecting iso-osmolar contrast at 37 °C through the guiding catheter.

OCT image analysis was performed using the Lightlab imaging software. The cross-section with the smallest lumen area and the reference cross section (frame with the largest lumen within 10 mm proximal or distal to MLA and before any side branch) were selected for analysis. The MLA and MLD were measured at the cross section with smallest lumen area. Reference lumen area (RLA) was measured at reference cross section. %AS was computed as: (RLA – MLA)/(RLA) × 100. The region around the MLA where the lumen area is less than 50% of the reference lumen area was taken as stenosis length.

Fibrous (homogeneous, signal-rich region), calcified (signal-poor region with defined edges), and lipid (signal-poor region with diffuse edges) plaques were identified using FD-OCT. Sudden attenuation of signal behind thin diffuse fibrous cap was considered highly suggestive of vulnerable plaque.

The statistical analysis was performed using Medcalc software version 12.5 (Ostend, Belgium). Continuous variables are expressed as mean ± standard deviation and categorical variables are expressed as percents. The relationships between FFR- and FD-OCT-derived parameters were analyzed using linear and non-linear regression analysis to determine the correlation coefficients between FFR and FD-OCT. A p-value <0.05 was considered as significant. The receiver operating characteristics (ROC) curve analysis, which includes estimation of area under the curve (AUC), determination of optimal cut-off value to predict an FFR ≤ 0.8, and related sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), was performed to determine the diagnostic efficiency of FD-OCT in identifying severity of stenosis. The diagnostic efficiency was classified according to AUC values as low (less than 0.70), moderate (0.70–0.90), and high (greater than 0.9) [21].

Fig. 1A shows angiographic view of an intermediate coronary stenosis. Fig. 1B1–B4 shows OCT cross-sectional images with measured lumen dimensions at various locations. Fig. 1C shows the longitudinal OCT reconstruction of the artery showing the stenosis and locations of OCT cross sectional images (B1–B4).

Results

The measurements related to 41 coronary stenoses in 30 patients were analyzed with FFR, QCA, and FD-OCT. The clinical data and stenosis characteristics obtained through QCA and FD-OCT are presented in Table 1. The mean age of the patients was 64 ± 11 years, and 24 patients (80%) were male. The mean MLA and MLD by OCT were 2.53 ± 0.92 mm^2 and 1.41 ± 0.37 mm respectively. The FFR value was ≤0.80 in 10 stenoses (24.4%). The comparative analysis in FD-OCT measurements between stenosis with FFR > 0.80 and those with FFR ≤ 0.80 are presented in Table 2.

The relationship between FFR- and FD-OCT-derived lumen measurements are presented in Fig. 2A–C. A poor but significant correlation between FFR- and FD-OCT-measured MLA ($r^2 = 0.4$, $p < 0.001$), MLD ($r^2 = 0.28$, $p < 0.001$), and %AS ($r^2 = 0.13$, $p = 0.02$) was found. The ROC curves for FD-OCT-measured MLA and MLD are presented in Fig. 3A and B. In the overall group, the diagnostic efficiency of MLA and MLD in identifying significant stenosis was moderate. The area under the curve (AUC) was 0.80 [95% confidence interval (CI): 0.64–0.91] for MLA and 0.76 (95% CI: 0.60–0.88) for MLD. Low diagnostic efficiency was found for FD-OCT-derived %AS (AUC: 0.63, 95% CI 0.46–0.79). The best cut-off values of OCT measured lumen parameters to identify stenosis with FFR ≤ 0.80 were 1.62 mm^2 (specificity 97%, sensitivity 70%, PPV 89%, and NPV 91%) for MLA and 1.23 mm (specificity 87%, sensitivity 70%, PPV 64%, and NPV 90%) for MLD.

When the stenoses were divided according to vessel reference diameter of 3 mm, 21.2% (7 of 33) of small-vessel stenoses and 25% (2 of 8) of large-vessel stenoses had FFR value ≤0.8. To assess the influence of vessel size on the ability of FD-OCT to identify severe coronary stenoses, we analyzed the subgroup of stenoses located in vessels having diameter <3 mm as measured by QCA. The ROC