Feasibility of Intracoronary Frequency Domain Optical Coherence Tomography Derived Fractional Flow Reserve for the Assessment of Coronary Artery Stenosis

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SUMMARY

Frequency domain optical coherence tomography (FD-OCT) provides cross-sectional images of coronary arteries and deployed stents with micron resolution and measures lumen dimensions with excellent reproducibility. FD-OCT combined with a blood flow resistances model can overcome many limitations of conventional measures of stenosis severity based on quantitative coronary angiography (QCA) and intravascular ultrasound (IVUS). The aim of this feasibility study was to investigate the relationship between pressure derived fractional flow reserve (FFR) and FD-OCT derived FFR, a new method for quantitative measure of stenosis severity that estimates the blood flow resistance and microvascular resistance of the vessel segments imaged by FD-OCT. A total of 26 coronary stenoses in 20 patients were studied consecutively with QCA, pressure derived FFR, and FD-OCT. There was a moderate but significant correlation between pressure derived FFR and FD-OCT derived FFR ($r = 0.69$, $P < 0.001$). Bland-Altman analysis showed that the mean differences between pressure derived FFR and FD-OCT derived FFR were $0.05 \pm 0.14$ (limits of agreement: -0.09 to 0.19). The root mean square error (RMSE) between FD-OCT derived FFR and pressure derived FFR was found to be $\pm 0.087$ FFR units. FD-OCT derived FFR has the potential to become a valuable tool for the assessment of coronary artery stenosis. (Int Heart J 2014; 55: 307-311)

Key words: Lesion assessment, Coronary stenosis, Blood flow resistance

Fractional flow reserve (FFR), measured with a pressure wire, is considered as the physiology standard in the functional assessment of intermediate coronary stenosis. Intracoronary optical coherence tomography (OCT) provides cross-sectional images of coronary arteries and deployed stents with resolution 10-15 times higher than intravascular ultrasound (IVUS). OCT is used for anatomic and morphologic assessment of coronary stenosis and provides lumen measurements with excellent reproducibility. OCT also provides information about plaque vulnerability, calcification, and other parameters which helps in guiding the procedure along with diagnostics. The frequency domain OCT (FD-OCT) systems provide faster image acquisition speeds, higher frame rates, and greater scan depths as compared to time domain OCT (TD-OCT) systems. FD-OCT combined with a blood flow model can overcome many limitations of conventional measures of stenosis severity based on QCA and IVUS. The main objective of this feasibility study was to investigate the potential of FD-OCT derived FFR for the assessment of coronary artery stenosis. Through the volumetric analysis of FD-OCT images, FFR was calculated from the blood flow resistance and the microvascular resistance. A comparison between FD-OCT derived FFR and pressure derived FFR was also conducted in this study.

METHODS

A total of 26 coronary stenoses in 20 patients with stable angina and/or ischemia documented on exercise stress test were studied consecutively with QCA, pressure derived FFR, and FD-OCT during diagnostic coronary angiography. The study was approved by Galway clinical research ethics committee and informed consent for all procedures was obtained from each patient. Eligible patients had a single de novo stenosis in a native coronary artery with diameter stenosis > 30% and lesion length ≤ 25 mm by visual estimation. Patients with an additional stenosis in a second coronary artery were also eligible if the other inclusion criteria were fulfilled. Main exclusion criteria were multiple stenoses in the target vessel, bypass graft stenosis, left main stenosis, and stenosis located in diseased vessels of acute coronary syndrome.

Coronary angiograms were obtained in multiple orthogonal views after intracoronary nitrates (100 μg). The reference vessel diameter (RVD), lesion length (LL), percent diameter stenosis (%DS), percent area stenosis (%AS), and minimal lumen diameter.
men diameter (MLD) were measured using validated QCA software (CASS II, Pie Medical Imaging, BV, Maastricht, The Netherlands).

Pressure derived FFR, which is the ratio of the intracoronary pressure to the aortic pressure, was measured using a coronary pressure guide wire (St. Jude Medical, San Diego, CA) at maximum hyperaemia induced by intravenous adenosine, managed at 140 μg/kg/min through a large peripheral vein. Stenoses were considered severe if FFR ≤ 0.80.

A commercially available FD-OCT system (C7XR) and the Dragonfly catheter (St. Jude Medical, Lightlab Imaging Inc., Westford, MA, USA) were used for the OCT imaging of the stenosis. A pullback speed of 0.2 cm/s was used and the blood was cleared by injecting iso-osmolar contrast at 37°C through the guiding catheter.

Lightlab Imaging software was used for the FD-OCT image analysis. The minimum lumen area (MLA) and MLD were measured at the cross section with the smallest lumen area. Proximal and distal reference segments of the target stenosis were identified manually by the contour of the lumen. The lumen areas and diameters were measured at the proximal and distal reference cross sections (frames with the largest lumen areas). The volumetric blood flow resistance and microvascular resistance of each stenosis segment were computed from the cross-sectional lumen areas and diameters obtained from FD-OCT pull back images.

The calculation of FD-OCT derived FFR is based on a blood flow model. In this model the blood flow driven by the difference between the arterial pressure and the coronary venous pressure is limited by the total flow resistance of the branch which is composed of microvascular resistance under maximal hyperaemia (R_{mv}), blood flow resistance of the stenosis (R_s), and the blood flow resistance of the length of vessel outside the imaged segment (R_e). FFR was computed as: \((R_{mv} + R_e) / (R_{mv} + R_s + R_e)\). \(R_{mv}\) was calculated by dividing the hyperaemic microvascular resistance index (h-MRv), set equal to the minimum value measured by Doppler flowmetry in previous studies (100 mmHg·s/cm³), by the cross-sectional area of the proximal reference segment. R_s was calculated as the viscous flow resistance of the length of vessel outside the imaged segment using Poiseuille’s law assuming that the entire vessel had a fixed length of 8 cm and a cross-sectional area equal to the average of the proximal and distal reference cross-sectional areas. R_e was calculated using the analytical method developed by Kirkeeide, Gould and others. R_s is assumed to consist of a flow independent component that results from viscous losses and a flow dependent component that results from kinetic losses.

Medcalc software version 12.5 (Ostend, Belgium) was used for statistical analysis. Linear regression analysis was performed to determine the correlation between pressure derived FFR and FD-OCT derived FFR. A \(P\) value < 0.05 was considered as significant. Bland-Altman analysis was performed to compare the measurements obtained from FD-OCT and pressure derived FFR.

Figure 1 (A1 to A3) shows OCT cross sectional images with measured lumen dimensions at various locations. A1: Proximal reference segment. A2: Minimal lumen segment. A3: Distal reference segment. B: Longitudinal OCT reconstruction of the artery showing locations of OCT cross sectional images (A1 to A3). C: Pressure derived FFR measurement for coronary stenosis. In this figure, Pa is proximal to the lesion pressure and Pd is distal to the lesion pressure, FFR value is calculated as the ratio of Pd and Pa.
RESULTS

The measurements related to 26 coronary stenoses in 20 patients were analyzed with QCA, pressure derived FFR, and FD-OCT. The patient characteristics are presented in Table I. The mean age of the patients was 62 ± 12 years and 15 patients (75%) were male. A total of 17 patients (85%) had hypertension and 7 (35%) had diabetes mellitus. The stenosis characteristics are presented in Table I. The left anterior descending artery (LAD) was the most common studied vessel (16 stenoses, 61.5%). QCA analysis was performed for all study stenoses (Table II). The average RVD, LL, MLD, %DS and %AS were 2.09 ± 0.59 mm, 8.26 ± 4.5 mm, 1.35 ± 0.57 mm, 45 ± 11.1%, and 68 ± 12.4%, respectively. The results of the FD-OCT measurements are presented in Table III. The mean MLA, MLD and %AS by OCT were 2.42 ± 1.07 mm², 1.41 ± 0.37 mm, and 64 ± 13%, respectively.

Figure 2A shows the linear regression analysis for pressure derived FFR and FD-OCT derived FFR. There was a moderate but significant correlation between pressure derived FFR and FD-OCT derived FFR (r = 0.69, P < 0.001). Figure 2B shows the Bland-Altman analysis for pressure derived FFR and FD-OCT derived FFR. The mean differences between the measurements were 0.05 ± 0.14 (limits of agreement: -0.09 to 0.19). The root mean square error (RMSE) between FD-OCT derived FFR and pressure derived FFR was found to be ±0.087 FFR units.

DISCUSSION

The main findings of this study are that there is a significant correlation between FD-OCT derived FFR and pressure derived FFR. The FD-OCT derived FFR based on blood flow resistance and hyperaemic microvascular resistance explains the roles of the variables that lie behind the relationship between anatomical and functional measures of stenosis severity.

The decision making on revascularization for severe coronary stenosis (having stenosis diameter > 70% on angiography) is mostly based on the interpretation of the coronary angiogram, but the assessment of intermediate coronary stenosis, defined angiographically as 40% to 70% luminal narrowing, via an angiogram or quantitative coronary angiography (QCA) is imprecise. The evaluation of such stenosis using pressure derived FFR results in excellent clinical outcome, but some operators prefer to use IVUS or OCT as they provide additional information and instrumental data on the sufficiency of stent implantation. OCT has better efficiency and sensitivity although it has a lower penetration depth than IVUS.

The ILUMEIN system (St. Jude) used in this study combines FD-OCT imaging and pressure derived FFR into one platform which helps optimise the use of percutaneous coronary intervention when treating patients suffering from ischemia. This system features pressure wire (Aeris, a wireless instrument that measures FFR to assess the stenosis severity, Wi-Box, a wireless device that receives aortic pressure readings wirelessly, and the FD-OCT imaging system (C7-XR) which provides high resolution images up to 10 μm, image acquisition rate up to 0.25 cm/sec, frame rate of 100 frames/s, and scan diameter of 10 mm. The FD-OCT system used in this study acquires images without any balloon occlusion. Balloon occlusion used in the TD-OCT technique reduces the intracoronary perfusion pressure and results in underestimation of the lumen measurements.
Stefano, et al\(^{(18)}\) were the first to determine the correlation between FFR and OCT derived lumen measurements in 14 patients with 18 stenoses. They found no significant correlation between FFR and the OCT measured MLA (\(r = 0.167, P = 0.56\)), MLD (\(r = -0.42, P = 0.13\)), and %AS (\(r = 0.29, P = 0.29\)). Recently, Gonzalo, et al\(^{(19)}\) evaluated the diagnostic efficiency of OCT derived lumen measurements in identifying the stenosis severity in 56 patients with 61 stenoses. They reported poor but significant correlation between FFR and OCT measured MLA (\(r = 0.51, P < 0.001\)), MLD (\(r = 0.4, P = 0.005\)), and %AS (\(r = 0.33, P = 0.02\)). FD-OCT derived FFR in the present study correlates more closely with pressure derived FFR than the FD-OCT measured anatomical parameters MLA, MLD, and %AS and has potential clinical advantages.

In this study a relatively small RMSE (± 0.087 FFR units) was found between FD-OCT derived FFR and pressure derived FFR. The improved predictive ability of FD-OCT derived FFR compared to MLA, MLD, and %AS can be credited to the excellent lumen measurement capability of FD-OCT, combined with blood flow model. The principles that lie behind computation of image analysis based FFR can also be applied to IVUS, but the accuracy of measuring lumen dimensions in tight stenoses may limit its ability in this application.

Koo, et al\(^{(20)}\) predicted FFR values noninvasively using coronary computed tomography. The predicted FFR values were based on a computational flow model and showed significant improvements over single cross-sectional measurements. The achieved RMSE of 0.116 FFR units in their study was bigger than the RMSE (± 0.087 FFR units) achieved with FD-OCT derived FFR in the present study.

The present study was exploratory in nature and the presented results include a limited population size so further investigations are needed to confirm the results. Although the study includes stenoses in the major coronary arteries, the methods for calculating blood flow resistances may not hold in all locations of the coronary vasculature. Furthermore, the number of patients studied was too small to derive meaningful cut-off values for stenting decisions so the FD-OCT derived FFR introduced in this study should not be considered as a substitute for pressure derived FFR in primary stenting decisions. Although FD-OCT derived FFR may address several limitations of conventional measures of stenosis severity based on QCA and IVUS, it does not take into account variations in myocardium mass and hyperaemic response.

**Conclusions:** FD-OCT derived FFR, a quantitative measure of stenosis severity, showed a significant correlation with pressure derived FFR. With further validation and development, FD-OCT derived FFR has the potential to become a valuable tool for the assessment of coronary artery stenosis and may help with interventional procedural planning and decision making.

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**References**