# Correlation of Optical Coherence Tomography-Derived Variables with Fractional Flow Reserve (≤0.8) in Patients with Coronary Artery Stenosis: An Observational Study

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## Abstract

**Objective:** The present study was designed to establish the correlation between anatomical variables analyzed using optical coherence tomography (OCT) and physiological assessment provided by fractional flow reserve (FFR, ≤0.8) in patients with significant coronary artery stenosis. **Materials and Methods:** This was a prospective, single-center observation study which included total fifty patients who were diagnosed with coronary artery disease in the presence of significant stenosis (>70%) as per coronary angiography. The FFR ≤0.8 was considered as positive with severe stenosis. Minimal luminal area (MLA), minimal luminal diameter (MLD), percent area stenosis, and percent diameter stenosis were calculated as OCT variables in all patients. **Results:** The mean age of the patients was 56 ± 7.13 years. The mean FFR was found to be 0.72 ± 0.06. The OCT-derived MLA was 1.97 ± 0.53 mm$^2$ and MLD was 1.35 ± 0.22 mm. The Pearson correlation coefficients of OCT-derived MLA (cutoff: 2 mm$^2$) and MLD (cutoff: 1.24 mm) with FFR were 0.21 ($P < 0.05$) and 0.03 ($P < 0.05$) with 67% and 71% diagnostic efficiency, respectively. **Conclusion:** The study identified a significant correlation between OCT-derived MLA (poor)/MLD (moderate) and FFR (≤0.8). Thus, both the techniques, when performed collectively, provide valuable information regarding coronary artery morphology and physiology.

**Keywords:** Coronary artery disease, fractional flow reserve, optical coherence tomography, plaque morphology

## Introduction

In India, the prevalence of coronary artery disease has increased significantly over the past few decades accounting for 30%–40% of deaths. Coronary angiography, though a gold standard, has documented several limitations demanding the use of more advanced imaging techniques such as fractional flow reserve (FFR) for functional and optical coherence tomography (OCT) and/or intravascular ultrasonography (IVUS) for anatomical assessment of coronary arteries.[1-3]

The FFR, a well-established physiological index, assesses the functional significance of coronary stenosis. Previously, FFR <0.75 was considered as an accurate predictor of ischemia. However, recently FFR ≤0.80 has been used as the optimal cutoff point to guide revascularization.[4] Although FFR provides good predictive values to make clinical decision, it does not provide morphological and anatomical information. Thus, imaging techniques such as IVUS and OCT should be used to evaluate the hemodynamic severity and morphology of coronary artery lesions.

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The OCT relies on the backscattering of light (wavelength – 1300 nm) to obtain cross-sectional images of tissue and has a 10-fold higher image resolution (axial and lateral) than IVUS. Thus, OCT provides accurate characterization of plaque morphology and composition in real time including thin fibrous caps, lipid pools, and fibrocalcific plaques.[5] Several investigators have reported different multimodality imaging using OCT and FFR and reported a correlation between FFR values and various anatomical parameters derived from OCT.[6,7] However, the differences in inclusion criteria and anatomical variables resulted in the different cutoff values of minimal luminal area (MLA) and minimal luminal diameter (MLD) for ischemic FFR. Thus, the purpose of this study was to establish the correlation of anatomical assessment obtained by OCT and physiological assessment provided by FFR in patients with significant coronary artery stenosis.

## Materials and Methods

This was a prospective, single-center observation study conducted at a tertiary care center in India. The study included total fifty patients who underwent coronary angiography and diagnosed with coronary artery disease with the presence of significant stenosis (>70%). Patients with diffuse coronary artery disease, ST-elevation myocardial infarction with cardiogenic shock or onset within 1 month, tandem coronary lesions, and with previously grafted vessels were excluded from the study. Furthermore, culprit vessel in acute coronary syndrome was excluded, and only nonculprit vessels were included in the study. All the patients underwent standard coronary angiography according to hospital protocol, and each lesion was analyzed in at least two different orthogonal views. The study was approved by the Institutional Ethics Committee and was conducted as per the Declaration of Helsinki. The written informed consent was received from all the included patients.

The FFR was recorded using pressure sensor guidewire (St. Jude Medical, St. Paul, Minnesota, USA). During measurement of FFR, hyperemia was induced with intracoronary adenosine (100 μg bolus) injection. The FFR was calculated as the ratio of distal coronary pressure to aortic pressure during maximal hyperemia. The FFR ≤0.8 was considered as positive with severe stenosis.

The OCT analysis was performed using intracoronary Fourier (Frequency)-domain OCT (FD-OCT) by introducing a small (2.7 French) imaging catheter over a guidewire (0.014”) distally into the coronary artery using standard guide catheters (6F or larger). A motorized pullback was performed to scan the coronary artery segment with a speed of 20 mm/s and a frame rate of 100 frames/s. OCT parameters, such as MLA, MLD, percent area stenosis, percent diameter stenosis, and lesion length, were determined in all patients with FFR ≤0.8.

The statistical analysis was performed using the Statistical Package for the Social Sciences Program (SPSS Inc., Chicago, USA), version 20. Categorical variables are stated as frequency-percentage and continuous variables are stated as mean ± standard deviation. The relationship between FFR and OCT-derived parameters was analyzed using Pearson correlation coefficient. $P < 0.05$ was considered as statistically significant. The receiver operating characteristics (ROC) curve was analyzed to determine the optimal cutoff values of MLA and MLD to predict FFR ≤0.8 and to estimate the area under the curve (AUC). The diagnostic efficiency of OCT parameters was classified according to AUC values as low (<0.7), moderate (0.7–0.9), and high (>0.9).

## Results

The study included 50 patients with significant (>70%) coronary artery stenosis in one of the major coronary arteries. The mean age of the study population was 56 ± 7.13 years with 37 (74%) males and 13 (26%) females. Total 50 significant lesions were diagnosed in 50 patients. Among all, 18 (36%) lesions were in the right coronary artery, 16 (32%) in the left anterior descending artery, 12 (24%) in the left circumflex artery, and 4 (8%) in the left main coronary artery. The demographic data and lesion characteristics of all patients are depicted in Table 1.

The FFR measurement depicted FFR ≤0.8 for all lesions followed by OCT analysis in all 50 patients. The mean FFR was found to be 0.72 ± 0.06. The characteristics identified using OCT are depicted in Table 2. In left main coronary lesions, the mean MLA was found to be 1.44 mm$^2$ and mean MLD was 1.19 mm.

The Pearson correlation coefficients of OCT-derived MLA and MLD with FFR were 0.21 ($P < 0.05$) and 0.03 ($P < 0.05$), respectively. Furthermore, the ROC curve

**Table 1: Baseline and clinical characteristics of all the patients**

| Parameters | Patients (*n*=50) |
|---|---|
| Age (years), mean±SD | 56.08±7.13 |
| Male, *n* (%) | 37 (74) |
| Hypertension, *n* (%) | 15 (30) |
| Diabetes mellitus, *n* (%) | 12 (24) |
| Smoking, *n* (%) | 14 (28) |
| Family history of CAD, *n* (%) | 6 (12) |
| Clinical presentation, *n* (%) | |
| Stable angina | 28 (56) |
| Unstable angina | 8 (16) |
| NSTEMI | 8 (16) |
| STEMI | 6 (12) |
| Vessel investigated, *n* (%) | |
| LAD | 16 (32) |
| RCA | 18 (36) |
| LCX | 12 (24) |
| LM | 4 (8) |

STEMI: ST-elevation myocardial infarction, NSTEMI: Non-STEMI, LAD: Left anterior descending, RCA: Right coronary artery, LCX: Left circumflex, LM: Left main analysis of OCT-derived MLA with FFR revealed AUC of 0.67 (confidence interval [CI]: 0.52–0.83), which suggested low but significant diagnostic efficiency of OCT-derived MLA to predict significant FFR (cutoff value: 2 $mm^2$) [Figure 1]. Similarly, the ROC curve of OCT-derived MLD with FFR showed AUC of 0.71 (CI: 0.43–0.98), which also suggested moderate diagnostic efficiency of OCT-derived MLD to predict significant FFR (cutoff value: 1.24 mm) [Figure 2]. The present study found that percent area stenosis has moderate efficiency to predict significant FFR with 64% sensitivity and 99% specificity to identify hemodynamically significant coronary lesions. In addition, this study also revealed that OCT-derived percent diameter stenosis has moderate diagnostic efficiency (71%) to predict significant FFR and reported that percent diameter stenosis has been associated with significant FFR in most of the situations.

**Table 2: Optical coherence tomography and fractional flow reserve characteristics of all the patients**

| Parameters | Number of lesions=50 (mean±SD) |
|---|---|
| OCT stenosis characteristics | |
| Minimal lumen area ($mm^2$) | 1.97±0.53 |
| Minimal lumen diameter (mm) | 1.35±0.22 |
| Reference lumen area ($mm^2$) | 9.80±1.81 |
| Reference lumen diameter (mm) | 3.27±0.378 |
| Area stenosis (%) | 79.29±5.70 |
| Diameter stenosis (%) | 57.71±7.61 |
| Length of lesion (mm) | 13.66±6.76 |
| Physiological parameter | |
| Mean FFR | 0.72±0.06 |

OCT: Optical coherence tomography, FFR: Fractional flow reserve, SD: Standard deviation

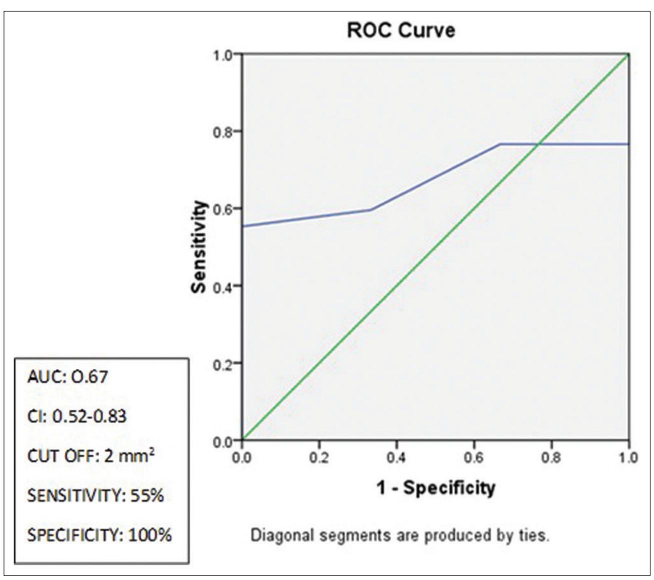


**Figure 1:** Receiver operating characteristics for optical coherence tomography-derived mean lumen area to predict fractional flow reserve ≤0.80

## Discussion

The differences between functional and anatomical evaluation of coronary stenosis have been under debate over the past two decades. The combination of anatomical and physiological information provided by OCT and FFR can be extremely useful in decision-making and guiding intervention.

In the present study, the cutoff value of OCT-derived MLA was 2.0 $mm^2$ with 55% sensitivity and 100% specificity. Therefore, MLA >2.0 $mm^2$ may be useful to exclude FFR ≤0.80. Furthermore, the cutoff value of OCT-derived MLD was 1.24 mm with moderate diagnostic efficiency (70%). Several studies assessing the diagnostic efficiency of IVUS in identifying stenosis severity, as determined by FFR, have demonstrated the different optimal cutoff values for MLA (2.0–4.0 $mm^2$) according to the reference lumen areas (5.5–11.9 $mm^2$) to predict the functional significance of coronary stenosis, which were found quite higher than OCT-derived values.[8-12] The mean reference lumen area in the present study was 9.8 $mm^2$ and reference diameter was 3.27 mm. Stefano *et al*.[7] first described the potential complementary role of OCT and FFR to guide decision-making in the evaluation of coronary artery stenosis. Moreover, Shiono *et al*.[13] evaluated the diagnostic efficiency of OCT-derived lumen measurements in identifying severe coronary stenoses in 59 patients with 62 lesions. That study reported 1.91 $mm^2$ as an ideal cutoff value for MLA with moderate diagnostic efficiency, however, the cutoff used for functional relevance was low (FFR < 0.75) and OCT measurements were performed using time-domain (TD) occlusion technique. The balloon occlusion used in the TD-OCT technique reduces the intracoronary perfusion pressure and results in underestimation

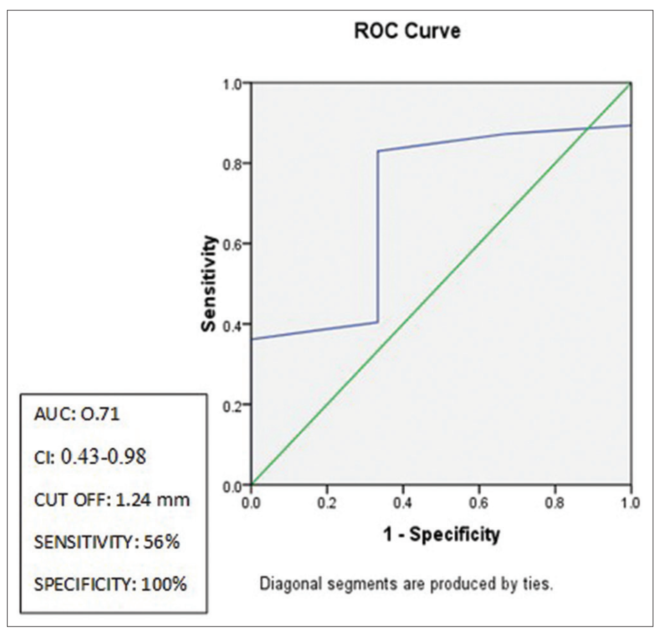


**Figure 2:** Receiver operating characteristics for optical coherence tomography-derived mean lumen diameter to predict fractional flow reserve ≤0.80

of the lumen measurements. FD-OCT system used in the study does not require any balloon occlusion for image acquisition and thus offer assessment with more accuracy. However, Shiono *et al*.[13] found a significant correlation between OCT-derived MLA and FFR with 93.5% sensitivity, 77.4% specificity, 85.4% accuracy, and diagnostic efficiency of 90%. Likewise, the present study also reported a significant but weak correlation between FFR and OCT-derived MLA with 55% sensitivity, 100% specificity, and 67% diagnostic efficiency.

Furthermore, Gonzalo *et al*.[14] evaluated the diagnostic efficiency of OCT-derived lumen measurements in identifying the stenosis severity. They reported 1.95 $mm^2$ as a cutoff value for MLA which was diagnosed with 74% efficiency (AUC). In a study by Zafar *et al*.,[15] a poor but significant correlation between FFR and FD-OCT-derived MLA ($r^2 = 0.4$, $P < 0.001$), MLD (correlation coefficient, $r^2 = 0.28$, $P < 0.001$), and percent area stenosis ($r^2 = 0.13$, $P = 0.02$) was observed. In our study, we also found a weak correlation between FFR and OCT-derived MLA ($r^2 = 0.21$, $P < 0.05$) and MLD ($r^2 = 0.02$, $P < 0.05$). They use the cutoff value of 1.62 $mm^2$ (sensitivity 70% and specificity 97%) for MLA and 1.23 mm (sensitivity 70% and specificity 87%) for MLD to predict significant FFR. However, we found a cutoff value of 2.0 $mm^2$ for MLA (sensitivity 55% and specificity 100%) and 1.24 mm for MLD (sensitivity 56% and specificity 100%). The lower cutoff value of MLA in their study may be due to lower mean lumen reference area (7.35 $mm^2$) as compared to our study (9.8 $mm^2$) as various characteristics of vessel such size, location, diameter, lesion location, and artery distribution (left vs. right coronary artery) influence the final result of the analysis.

### Study limitations

The major limitation of the present study is small study population ($n$ = 50) and lack of follow-up; thus, further randomized controlled study with a large sample and long-term follow-up is warranted to provide more evidence to support the strategy. The proportion of diabetic and nondiabetic patients is not balanced as most diabetic patients have diffuse disease. In the present study, only four patients of left main coronary stenosis were included, and thus, OCT parameters cannot predict significant FFR in such patients.

## Conclusion

There were a poor but significant correlation between FFR and OCT-derived MLA and a moderate correlation between FFR and OCT-derived MLD in patients with significant coronary lesions. Thus, both the techniques, when performed collectively, provide valuable information regarding coronary artery morphology and physiology and also act as a helpful guide before performing revascularization into stenosed coronary artery. However, further randomized controlled study with a large sample size and long-term follow-up is required to generate more evidence to support the strategy.


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Nil.

### Conflicts of interest

There are no conflicts of interest.


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