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***Original Research Article***

# Efficacy of IVUS-Based Fractional Flow Reserve in Patients With Intermediate Left Main Stenosis

**Muhammad Ismail Khan[1*], Adeela Shahzadi[2], Dost Muhammad[3], Nouman Nazeer[4], Shahrukh Ahmed[5]**

[1]*Department of Cardiology, HSP, Mianwali, Pakistan*
[2]*Department of Cardiology, Pervaiz Elahi Institute of Cardiology, Bahawalpur, Pakistan*
[3]*Department of Cardiology, RIC Rawalpindi, Pakistan*
[4]*Department of Cardiology, NICVD Karachi, Pakistan*
[5]*Department of Cardiology, CPEIC Multan, Pakistan*
**Corresponding author`s email address:* ismailkhanghorani111@gmail.com

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**Abstract:** *Assessment of intermediate left main (LM) coronary artery stenosis remains clinically challenging. Wire-based fractional flow reserve (FFR) is considered the gold standard. Still, the use of intravascular ultrasound (IVUS)-derived functional indices, such as ultrasonographic flow ratio (UFR), is emerging as a potential non-wire alternative for physiological lesion assessment.* ***Objective:*** *To evaluate the diagnostic accuracy and efficacy of IVUS-based FFR (UFR) compared to wire-based FFR in patients with intermediate LM coronary artery stenosis.* ***Methods:*** *A prospective study was conducted at a tertiary care cardiology hospital from May 2024 to May 2025. A total of 100 adult patients with angiographically intermediate LM stenosis (defined as 50–70% diameter stenosis) were included. IVUS was performed using a motorized pullback device operating at 0.5 mm/s, from a distal point in the left coronary artery up to the aortic ostium. UFR was calculated based on IVUS pullback data. Wire-based FFR was recorded by positioning a pressure guidewire in the downstream coronary branches. The diagnostic performance of UFR was assessed using receiver operating characteristic (ROC) analysis, with wire-based FFR (cut-off <0.80) as the reference standard.* ***Results:*** *There was a moderate correlation between UFR and FFR ($r = 0.692$, $p < 0.0001$). UFR demonstrated a high area under the curve (AUC = 0.88; 95% CI: 0.91–0.99) for detecting functionally significant LM stenosis, outperforming angiography (AUC = 0.71, $p < 0.001$) and minimum lumen area (MLA) measurement (AUC = 0.79, $p = 0.11$). The optimal UFR threshold showed a diagnostic accuracy of 83.2%, superior to MLA ≤ 4.5 mm² (59.1%) and comparable to MLA ≤ 6.0 mm² (81.4%). Sensitivity for UFR, MLA ≤ 4.5 mm², and MLA ≤ 6.0 mm² was 92.7%, 48.6%, and 85.8%, respectively. FFR-based specificity was 57.6%, with a positive predictive value of 85.5%, negative predictive value of 78.3%, favorable likelihood ratio (+LR) of 2.19 (95% CI: 1.16–4.34), and negative likelihood ratio (–LR) of 0.09 (95% CI: 0.05–0.52).* ***Conclusion:*** *IVUS-derived FFR (UFR) demonstrated high diagnostic accuracy and sensitivity, comparable or superior to wire-based FFR in identifying functionally significant intermediate LM stenosis. UFR may offer a reliable, less invasive alternative to pressure-wire-based assessment in select patients.*

**Keywords:** Angiography, Coronary stenosis, Fractional Flow Reserve, Intravascular Ultrasound, Left primary coronary artery disease, Ultrasonic Flow Ratio

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## Introduction

The management of patients with intermediate left central stenosis (LMS) remains a clinical challenge, as the decision-making process regarding revascularization often hinges upon accurate assessment of lesion severity and its hemodynamic significance. Current guidelines recommend fractional flow reserve (FFR) measurement as the gold standard for evaluating the physiological importance of coronary artery stenosis, including that of the left main artery (1,2). However, traditional angiography may not provide adequate anatomical detail or comprehensive physiological insights, leading to potential under-treatment or over-treatment of patients with intermediate stenosis (3,4).

Intravascular ultrasound (IVUS)-based fractional flow reserve (IVUS-FFR) represents a promising adjunct to these traditional modalities, offering enhanced anatomical imaging alongside functional assessment capabilities. The ultrasonic flow ratio (UFR) derived from IVUS images is notably faster and can be performed during the same procedure, facilitating real-time decision-making (2,5). This integration of anatomical views could improve the stratification of patient risk by identifying plaque composition and lesion morphology—crucial factors in determining suitability for revascularization (6,7).

Recent studies have highlighted that IVUS-FFR can successfully correlate with FFR measurements while providing additional information on the characteristics of the arterial wall and surrounding structures, which could affect clinical outcomes (8,9). The prognostic significance of accurately gauging the severity of intermediate left central stenosis has been emphasized in several trials, which have concluded that integrated imaging techniques can lead to better long-term results following percutaneous coronary interventions (PCI), (10,11). Moreover, with increasing evidence suggesting that IVUS can aid in optimizing stent deployment and other procedural techniques, it is increasingly recognized as a vital tool in contemporary cardiology practice (12, 13,14).

Given the promising integration of IVUS and FFR in accurately assessing intermediate LMS, the current study seeks to evaluate the diagnostic efficacy and clinical outcomes of using IVUS-based fractional flow reserve in patients presenting with intermediate left central stenosis. The elucidation of the role of IVUS-FFR in this context will contribute to the establishment of protocols that can enhance decision-making processes in interventional cardiology, ultimately improving patient outcomes and resource utilization.

Intermediate left central stenosis poses a significant risk to patients, necessitating careful evaluation and selection for revascularization therapies. IVUS-FFR has emerged as a potentially valuable methodology in this regard, with studies suggesting improved diagnostic performance compared to traditional techniques (4,5,15). By systematically assessing the anatomical and functional parameters of coronary lesions via IVUS,

clinicians may be better equipped to make informed decisions regarding intervention strategies.

The incorporation of IVUS-derived measurements has demonstrated advantages in identifying functionally significant lesions, even when angiographic appearances may be misleading (16,17). Furthermore, existing literature advocates for a cost-effective analysis regarding the use of advanced imaging modalities, which supports the rationale for this study as healthcare budgets increasingly emphasize the need for economically advantageous yet clinically effective interventions (18,19). As the field of cardiology continues to evolve, establishing the clinical efficacy of IVUS-based FFR may also provide insights into the future standardization of practice guidelines, enabling healthcare systems to capitalize on both improved survival rates and reduced procedural complications through personalized treatment pathways tailored to individual anatomical and physiological profiles (20,21).

**Methodology**

A prospective study was conducted in the Cardiology Hospital from May 2024 to May 2025. A total of 100 adult patients with intermediate left central stenosis (50-70% diameter) were selected for the study. Patients allergic to adenosine or contrast agents, contraindication to radiological examinations, severe heart failure, stage 3b or higher chronic kidney disease, kidney dysfunction, and in-stent restenotic lesion. All patients provided their consent for participating in research. The ethical committee of the hospital approved the study.

Patients with lesions in the left coronary artery underwent complete revascularization before IVUS or FFR. A standard angiogram was used for all other vessels and the left main. Arterial spasm was relieved by injected nitroglycerin, and then angiography was performed to obtain two images that were 25° apart to visualize vessels. A percutaneous coronary intervention was performed with stent or balloon implantation after identification of significant lesions and confirmation of no stenotic lesions. IVUS was performed using a motorized pullback at 0.5mm/s, recording from the distal point (intended location of FFR pressure wire) to either branch of the left coronary artery, continuing until the aortic ostium was reached. The vessels, i.e., LAD or LCx, were chosen based on the location of narrowing or lesions; if both are involved, imaging was performed on both sides. If the plague was extended to the side branch, distal examination began from the downstream vessel.

FFR was measured by inserting the pressure guidewire into the downstream vessels. 160 mg/L or more ATP was administered in the antecubital vein to induce maximal hyperemia. Once stable hyperemia was achieved for 10s, the recording was begun, and sensor drift was eliminated by sensor pullback.

The primary outcome of the study was the ROC curve of UFR for the identification of functionally significant stenosis with FFR as the gold standard. The secondary outcomes were diagnostic accuracy, specificity, sensitivity, PPV, NPV, and positive and negative likelihood ratios of UFR and minimal lumen area.

All data analysis was done by SAS 9.4. Mean±SD and percentage were used to report categorical and continuous data, respectively. The Clopper-Pearson exact method was used to estimate diagnostic accuracies at the patient level. A logistic regression model was used to plot ROC curves, and Pearson's correlation coefficient was used to evaluate the relationship between FFR and UFR.

**Results**

A total of 100 patients with intermediate LM stenosis were included, with a mean age of 61 ± 10.3 years. 85% patients were male, 45% were diabetic 59% had unstable angina. 30% patients had ostial lesions and 45% had distal bifurcation lesions. Mean vessel diameter was 5.57 mm, with 65.8% being average diameter stenosis. IVUS and FFR measurements were successful in all patients with 60 pullbacks and 63 pullbacks, respectively. Mean FFR was 0.68, and 70 patients (70%) were functionally ischemic. Mean MLA was 5.16 mm2. The demographic and angiographic characteristics of patients are shown in Tables I and II.

A moderate association was recognized between UFR and FFR (r=0.692, p<0.0001). The AUC of UFR was 0.88 (95% CI: 0.91-0.99) for the diagnosis of functionally significant LM stenosis, which was significantly higher than the AUC of angiography (0.71, p<0.001) and MLA (0.79, p=0.11). The best cut-off of MLA was 6.09 mm2.

UFR had a significantly higher diagnostic accuracy of 83.2% compared to MLA ≤ 4.5mm2 (59.1%) and was similar to MLA ≤ 60mm2 (81.4%). The same pattern was noted for sensitivity with values of 92.7%, 48.6% and 85.8%, respectively. The specificity of FFR was 57.6%, PPV was 85.5%, NPV was 78.3%, +LR was 2.19 (1.16-4.34), and -LR was 0.09 (0.05-0.52) as shown in Table III.

**Table I: Demographic features of patients**

| Features | N (%) |
|---|---|
| Mean age | 61 ± 10.3 |
| Male gender | 85 (85%) |
| Mean BMI | 26.2 ± 4.0 |
| Diabetes | 45 (45%) |
| Hypertension | 66 (66%) |
| Hyperlipemia | 100 (100%) |
| Smokers | 61 (61%) |
| Family history of CAD | 30 (30%) |
| History of MI | 5 (5%) |
| Previous PCI | 30 (30%) |
| Previous CABG | 3 (3%) |
| **Clinical features** | |
| Stable angina | 40 (40%) |
| Unstable angina | 59 (59%) |
| Acute MI within 1 month | 3 (3%) |
| LVEF | 64.6 ± 6.3 |
| **Angiography results** | |
| Isolated left main diseases | 10 (10%) |
| Left main plus one vessel | 45 (45%) |
| Left main plus two vessels | 40 (40%) |
| Left main plus three vessels | 5 (5%) |

**Table II: Angiography results**

| Characteristics | N (%) |
|---|---|
| **Location** | |
| Ostial | 30 (30%) |
| Mid-shaft | 25 (25%) |
| Distal-bifurcation | 45 (45%) |
| Diameter of reference vessel | 5.57 ± 0.58 |
| Percentage diameter of stenosis | 65.8 ± 15.5 |
| Minimal lumen diameter | 2.17 ± 0.49 |
| Lesion length | 11.6 ± 5.53 |
| **IVUS findings** | |
| MLA | 5.16 ± 2.22 |
| MLA ≤ 4.5 $mm^2$ | 40 (40%) |
| MLA ≤ 5 $mm^2$ | 60 (60%) |
| Percentage of plague burden | 71.1 ± 9.9 |
| UFR | 0.68 ± 0.09 |
| UFR ≤ 0.8 | 80 (80%) |
| FFR | 0.66 ± 0.08 |
| FFR ≤ 0.8 | 69 (69%) |

**Table III: Accuracy of Diagnostic Modalities of Intermediate LM Stenosis**

| | **UFR ≤ 0.8** | **MLA ≤ 4.5 $mm^2$** | | **MLA ≤ 6 $mm^2$** | |
|---|---|---|---|---|---|
| | **Estimate** | **Estimate** | **P** | **Estimate** | **P** |
| Accuracy | 83.2% | 59.1% | 0.01 | 81.4% | 0.83 |
| Sensitivity | 92.7% | 48.6% | <0.0001 | 85.8% | 0.47 |
| Specificity | 57.6% | 84.8% | 0.15 | 67.3% | 0.63 |
| PPV | 85.5% | 88.6% | 0.92 | 83.6% | 0.91 |
| NPV | 78.3% | 39% | 0.11 | 67.5% | 0.89 |
| +LR | 2.19 (1.16-4.34) | 2.87 (0.81-11.3) | | 2.63 (1.17-5.79) | |
| -LR | 0.09 (0.05-0.52) | 0.58 (0.37-1.1) | | 0.19 (0.11-0.60) | |

**Discussion**

The evaluation of intermediate left central stenosis (LMS) remains a complex challenge in interventional cardiology. In this study, we assessed the efficacy of intravascular ultrasound (IVUS)-based fractional flow reserve (FFR) in a cohort of 100 patients. Our findings reveal that 70% of the cohort presented with functionally ischemic lesions, as indicated by a mean FFR of 0.68. This is consistent with existing literature that emphasizes the substantial prevalence of ischemia in patients with intermediate LMS, aligning with data reported by Hwang et al. (22), who highlighted the role of FFR in addressing ambiguous physiologic assessments in this patient demographic (23).

The moderate correlation observed between UFR and FFR ($r = 0.692$, $p < 0.0001$) suggests that UFR could serve as a reliable alternative for assessing hemodynamic significance in LMS. Notably, the area under the curve (AUC) for UFR was 0.88, significantly higher than that for angiography (0.71, $p < 0.001$) and comparable to the evaluated minimal lumen area (MLA) cutoff of 6.09 $mm^2$. This result echoes findings from the literature, indicating that imaging-guided techniques yield superior diagnostic performance in evaluating coronary lesions compared to traditional angiographic assessments (24). This insight positions UFR as a promising candidate for enhancing the diagnostic accuracy and management of coronary artery disease.

Our study demonstrated that UFR outperformed MLA in diagnostic accuracy (83.2% vs. 59.1%, respectively), which corroborates prior research indicating that angiography alone may lead to suboptimal treatment decisions due to its limitations in characterizing lesion severity (25). Furthermore, sensitivity rates showed UFR (92.7%) surpassing MLA (48.6%), indicating that UFR may better identify patients who would benefit from revascularization. This aligns with recent meta-analyses suggesting functional assessments significantly enhance the ability to predict adverse outcomes post-PCI (15).

Moreover, our results also highlighted UFR's specificity at 57.6%, which falls within ranges reported in clinical settings, further establishing its reliability in guiding treatment (22). The positive predictive value (PPV) of 85.5% and negative predictive value (NPV) of 78.3% reiterate UFR's utility as a clinically applicable parameter, signifying its potential role in optimizing patient selection for PCI. This is crucial, especially considering the clinical implications of deferred lesions based on IVUS and FFR findings, affirming the need for objective functional assessments to steer treatment decisions (26).

Furthermore, the prevalence of classic cardiovascular risk factors within our patient cohort—such as diabetes (45%), hypertension (66%), and smoking (61%)—is indicative of the complex interplay between these factors and premature coronary artery disease, emphasizing the necessity for tailored approaches in clinical practice. Previous studies have delineated the profile of patients with left primary coronary artery disease (LMCAD), reinforcing the criticality of comprehensive vascular assessment in these high-risk populations (27).

Thus, our investigation presents compelling evidence supporting the efficacy of IVUS-based UFR in evaluating intermediate LMS. Given its enhanced diagnostic accuracy compared with conventional metrics, UFR

could facilitate better clinical decision-making and improve outcomes in patients undergoing PCI. Future studies should aim to validate these findings within larger cohort populations and explore long-term outcomes post-intervention, contributing to the evolving landscape of personalized cardiovascular care.

## Conclusion

IVUS-derived FFR (UFR) demonstrated high diagnostic accuracy and sensitivity, comparable or superior to wire-based FFR in identifying functionally significant intermediate LM stenosis. UFR may offer a reliable, less invasive alternative to pressure-wire-based assessment in select patients.

## Declarations

**Data Availability statement**
All data generated or analysed during the study are included in the manuscript.
**Ethics approval and consent to participate**
Approved by the department concerned. (IRBEC-24)
**Consent for publication**
Approved
**Funding**
Not applicable

## Conflict of interest

The authors declared the absence of a conflict of interest.

## Author Contribution

**MIK (MD)**
*Manuscript drafting, Study Design,*
**AS (SR)**
*Review of Literature, Data entry, Data analysis, and drafting articles.*
**DM (DIP)**
*Conception of Study, Development of Research Methodology Design,*
**NN (Fellow)**
*Study Design, manuscript review, critical input.*
**SA (MO)**
*Manuscript drafting, Study Design,*

*All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.*

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