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# Role of Functional Evaluation of Intermediate Coronary Artery Lesions with Fractional Flow Reserve in Clinical Decision Making

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## ABSTRACT

### Introduction

Coronary angiography often misjudges intermediate (50-70%) lesions. Fractional flow reserve (FFR) accurately assesses their physiological significance to safely guide revascularization. Addressing limited local evidence, this Nepalese study evaluates role of FFR in determining lesion severity and guiding treatment decisions.

### Methods

This quantitative, cross-sectional study evaluated 43 patients with intermediate coronary lesions undergoing coronary angiography (CAG) at the Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC), Institute of Medicine, over one year. Patients with prior fibrinolytic treatment, connective tissue disorders, or skip lesions were excluded. Initially, revascularization or medical management—was planned based on visual CAG stenosis. Next, resting full-cycle ratio (RFR) and fractional flow reserve (FFR) were measured. Significant lesions (FFR ≤0.80, RFR ≤0.89) received percutaneous coronary intervention (PCI); others received medical therapy. This study analysed how FFR/RFR altered initial visually-guided treatment plans.

### Results

This study evaluates 43 intermediate coronary lesions (median age 66; 74% male) mostly presenting with chronic coronary syndrome. It compared visually estimated treatment plans after CAG against RFR/FFR-guided management. Visual assessment planned medical therapy for 88% (n=38) and intervention (PCI) for 12% (n=5). Functional assessment altered management strategy in 18 cases, deferring all five initially planned interventions to medical therapy and upgrading 13 medical management cases to revascularization. Functional assessment with FFR/RFR optimizes revascularization decisions for intermediate coronary lesions.

### Conclusion

Functional assessment (FFR/RFR) prevents suboptimal treatment of intermediate lesions. By altering planned management after CAG in 18 cases (redirecting 13 to PCI and deferring 5 to medical therapy), FFR shows role in optimal revascularization.

### Keywords

*Coronary angiography (CAG); fractional flow reserve (FFR); intermediate coronary artery lesions; resting full cycle ratio (RFR).*

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## INTRODUCTION

Cardiovascular disease contributed 26.9% of total deaths in Nepalese adult aged 20 years and older.[1] Coronary angiography (CAG) is standard technique for guiding percutaneous coronary intervention (PCI) in patients with myocardial ischemia.[2] Up to 25% patient have intermediate coronary artery stenosis (angiographic stenosis between 50% to 70%) and uncertainty about need of revascularization.[3] Visual estimation in CAG can be misleading in lesions with 40–70% stenosis.[4] For evaluating physiological lesions and identifying myocardial ischemia, fractional flow reserve (FFR) has been regarded as an effective index and gold standard test.[2]

Evidence shows that revascularization of intermediate coronary artery stenosis should not be based on angiographic finding only as additional functional testing as FFR improves treatment and long term outcome. In a 15 year follow up study, rate of myocardial infraction was lower in group who were deferred angioplasty based on negative FFR.[5] Delaying the revascularization of intermediate lesions can be done safely with FFR.[6] In a study done in two tertiary care centers 72% and 51.2% of FFR negative lesions were left untreated.[6] In a Nepalese cohort study 70% of FFR-negative lesions were successfully deferred from revascularization.[7] FFR-guided treatments have been linked to better clinical outcomes, fewer needless revascularizations, and lower medical expenses.[8] Use of FFR is increasing in Nepal and is being done at Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC) and Shahid Gangalal National Heart Centre.[7] However there has not been adequate study to evaluate its usefulness. Thus this study aims to find role of FFR in functional assessment of intermediate coronary artery lesion for clinical decisison making.

## METHODS

This is a quantitative, cross-sectional study which included 43 patients with intermediate coronary lesions who underwent angiography at cardiology department at Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC), Institute of Medicine (IOM) over a period of 1 year. (January–December 2025). Non probability sampling was used. Ethical clearance was obtained from Institutional review committee (IRC) of Institute of Medicine (IOM). Sample size was calculated as 43 using formula for prevalence studies {,n= ($Z^2 \times p \times q$) /$d^2$ )} with prevalence(p) of 2.9% [1] , with 95% confidence interval and 5% margin of error. Written consent was obtained from patients Patients who had 50-70% stenosis in invasive CAG were included. Patients pretreated with fibrinolytic agents before angiography, with connective tissue disorder (Systemic lupus erythematosus, scleroderma, takayasu) and with skip coronary lesion were excluded. Clinical, demographic and laboratory data were collected from charts, history and clinical examinations. Following angiographic visual estimation of coronary stenosis, cases were assigned to either revascularization or medical management (deferred revascularization) group. Then guide catheter was engaged into the coronary ostium and the specialized pressure wire (Pressure Wire X Abbot) zeroed and calibrated. The pressure wire was advanced to position the transducer distal to the lesion. The pressure waveforms were recorded at rest and during maximal hyperaemia induced by either intravenous or intracoronary adenosine.[9] Automated pressures distal (Pd) and proximal (Pa) to coronary stenosis was obtained. RFR and FFR (Pd/Pa) were derived by the automated machine. RFR ≤ 0.89 and FFR ≤ 0.80 were taken as positive result [10] and proceeded with PCI. Medical management was done in FFR negative lesion. Continuous variables are presented as means and standard deviations or median. Categorical variables are reported as frequencies and percentages. Treatment strategies, determined by initial angiographic visual estimation and subsequent FFR/RFR-guided functional assessment, were presented graphically. For statistical analysis, SPSS 31.0 was used.

## RESULTS

Forty three cases who had intermediate coronary artery lesions underwent resting full cycle ratio (RFR). The median age was 66 years in which 32 (74%) were males and 11 (26%) were females. More than half of cases had history of Type 2 Diabetes, Hypertension dyslipidaemia and smoking. Ten patients (23%) had past history of MI and 14 (33%) had past history of PCI. Most common presenting symptom was angina on exertion 39 (91 %) followed by dyspnoea on exertion 28 (65

%).The mean LVEF was 51.8%. Key baseline characteristics are summarized in Table 1.

*Table 1. Baseline Characteristics*

| Demographics | Patients (N= 42) |
|---|---|
| Age (years) (median) | 66 years |
| Female | 11 (26%) |
| Male | 32 (74%) |
| Medical history | |
| DM | 25 (58 %) |
| HTN | 25 (58 %) |
| Dyslipidemia | 26 (60%) |
| CKD | 5 (12 %) |
| Cerebrovascular accident | 2 (5%) |
| Peripheral arterial disease | 5 (12%) |
| Smoking | 22 (51%) |
| Previous PCI | 14 (33 %) |
| Previous MI | 10 (23 %) |
| Presenting Symptoms | |
| AOE | 39 (91 %) |
| DOE | 28 (65 %) |
| Both AOE and DOE | 23 (53 %) |
| LVEF% (mean ± SD) | 51.8± 11.49 (58%) |

DM: diabetes mellitus; HTN: hypertension; CKD: Chronic kidney disease; PCI: percutaneous coronary intervention; MI: Myocardial infarction; AOE: Angina on exertion; DOE: Dyspnea on exertion; LVEF: left ventricular ejection fraction; SD: standard deviation

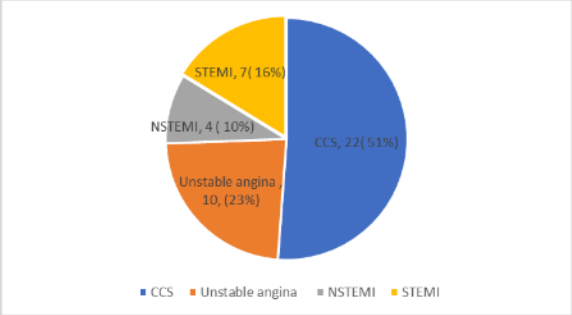


*Figure 1. Indication for Coronary Angiography.*

CCS: Chronic coronary syndrome; NSTEMI: Non ST elevation myocardial infraction; STEMI: ST elevation myocardial infraction.

RFR was done in 43 cases, while adenosine-induced FFR was carried out in 42 cases. One case had positive RFR and developed episode of bradycardia with hypotension suggestive of vasovagal symptoms so FFR with Adenosine was not done and stent was deployed and patient managed with intravenous fluid. For adenosine-induced hyperemia, intravenous approach was used in 8 (19%) patients and intracoronary approach in 34 (79%) patients. Procedural characteristics are summarized in Table 2.

*Table 2. Procedural characteristic*

| POST CAG PLAN | |
|---|---|
| Medical Management | 38 (88 %) |
| PCI | 5 (12%) |
| RFR | |
| POSITIVE | 13 (30%) |
| NEGATIVE | 30 (70%) |
| FFR | |
| POSITIVE | 12 (28%) |
| NEGATIVE | 30 (70%) |
| Not Done | 1 (2 %) |

Based on visual CAG estimation, 38 cases (88%) were planned for medical management and 5 (12%) for revascularization. Functional assessment yielded positive RFR and FFR results in 13 and 12 cases, respectively, while 30 cases tested negative.

*Table 3. Lesion distribution based on syntax score*

| SYNTAX SCORE | |
|---|---|
| SYNTAX < 22 | 24 (56%) |
| SYNTAX 22 - 33 | 17 (40%) |
| SYNTAX > 33 | 2 (4%) |

Out of forty three cases, coronary artery stent was placed in 13 (30%) case and Medical management done is 30 (70%) cases. Treatment plan after RFR/FFR on various coronary artery is shown in Figure 2.

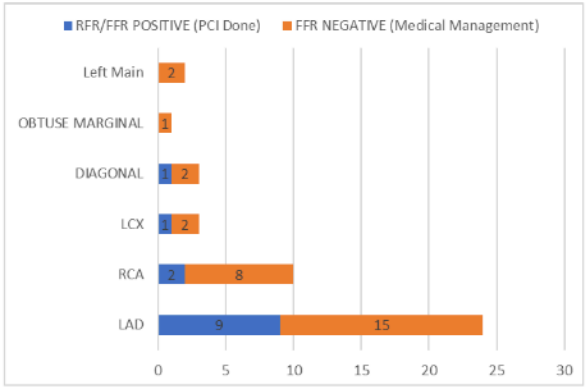


*Figure 2. Outcome of RFR/FFR based on coronary artery*

LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; LAD was most common Coronary Artery in which RFR and FFR was done 24 (56%) followed by RCA and LCX. In 2 cases of left main coronary artery stenosis angioplasty was deferred after negative FFR value.

Functional assessment (RFR/FFR) significantly reclassified initial treatment plans based on visual CAG. All five lesions initially planned for PCI — including 2 left main coronary artery lesions — were reclassified as hemodynamically non-significant, leading to deferred revascularization. Conversely, of the 38 lesions initially slated for medical management, thirteen (30%) demonstrated hemodynamically significant stenosis, prompting stent deployment. Figure 3 summarizes change in treatment plan pre and post RFR/FFR.

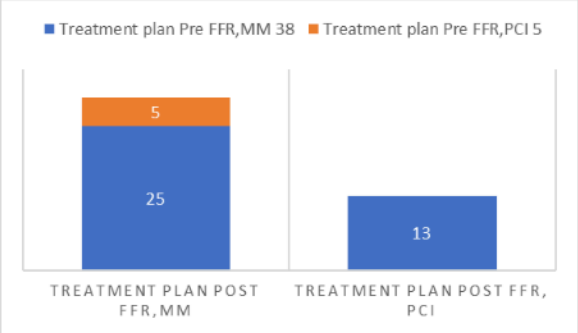


*Figure 3. Change in treatment strategy pre and post RFR/FFR*

MM: Medical management; PCI: percutaneous coronary intervention.

## DISCUSSION

The present study explores the use of FFR in identifying hemodynamic significance of intermediate coronary artery stenosis. It analyses the treatment plan made pre FFR by visual estimation of coronary stenosis with final treatment the patient received post FFR. The median age in this study was 66 years and majority of cases were males 32 (74%). The demographic profile was similar to other two studies done in Nepal where mean age of CAD was 63.5 years and 59.9 years with higher prevalence in males 52% and 76% respectively.[11] [12] Tobacco smoking was the main modifiable risk factor associated with CAD in this as well as previous studies done in Nepal.[13] In present study more than half of the cases had Type 2 diabetes, hypertension and dyslipidaemia among traditional risk factors for CAD. These are most prevalent comorbidity associated with CAD.[14] Hypertension in 80% and diabetes in 78% cases were present in CAD patients.[15] In this as well as other studies chest pain and dyspnoea were the hallmark presenting symptoms of CAD.[16] The most frequent manifestation of CAD was chronic coronary syndrome (CCS), which was followed by unstable angina, STEMI, and NSTEMI. CAD can present in a variety of ways, with CCS[17] being the more common manifestations.

The use of FFR has been recommended for evaluation of angiographic intermediate coronary lesions (50% to 70% stenosis) and for guiding revascularization decisions by the European (Class 1A)[18] and American guidelines (Class 2A).[9] Accordingly, FFR in the current study was utilized in patients with intermediate lesions. Wire-based fractional flow reserve (FFR) is a test designed to determine physiological significance of coronary artery stenosis.[19]

As per FAME Study lesions with FFR value < 0.8 underwent angioplasty as it significantly reduced the rate of the composite end point of death, nonfatal myocardial infarction, and repeat revascularization at 1 year.[2] There was no significant difference between intracoronary and intravascular adenosine for FFR.[20]

In the present study out of forty two intermediate lesions assessed, 13(30%) had significant RFR and FFR value and underwent revascularization, whereas 30(70%) had functionally non-significant stenosis with FFR > 0.8. In one study out of fifty eight intermediate lesions assessed, 17(29.31%) had significant FFR value, requiring revascularization and 41(70.69%) had functionally non-significant stenosis.[7] In another study 104 intermediate lesion were assessed by FFR and 43(41.3%) lesions had hemodynamic significance and 61(58.7%) lesions had no hemodynamic significance.[21]

The treatment strategy based on angiography changed post FFR in this study. Among the 38 lesions initially assigned to medical management, 13 underwent percutaneous coronary intervention (PCI) due to significant FFR values (<0.8). Conversely, non-significant FFR results led to the deferral of all 5 cases originally planned for PCI. In RIPCORD study 13% underwent and 28% were deferred revascularization with FFR data.[22] In DEFINE REAL Study initial (angiography guided) and final (post FFR) strategy of treatment was changed in 30% of patients with multivessel disease with intermediate lesion.[23] In FIND study post FFR, about 40% of lesions planned

for revascularization after angiography were spared from unnecessary revascularization.[24]

There are several limitations to this study. First, the study was conducted in a single centre and it remains to be seen if it can also be validated in other centres in Nepal. Second, the small sample size may limit the statistical power of the findings. More studies with larger sample size may further demonstrate the clinical role of FFR in optimizing revascularization in intermediate coronary lesions.

## CONCLUSION

This study evaluates the role of functional assessment on the management of intermediate coronary artery stenosis. Initial treatment plans based on visual estimation of CAG were reclassified following FFR/RFR evaluation in 18 cases. Specifically, thirteen cases (30%) initially planned for medical management were found to be hemodynamically significant and subsequently underwent PCI. Conversely, five cases initially slated for revascularization were hemodynamically non-significant, allowing for the deferral of PCI in favour of medical management. Thus FFR can be a useful tool to guide optimal coronary revascularization in intermediate coronary artery stenosis.

## CONFLICT OF INTEREST

No conflict of interest.

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