ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

Reclassification of Treatment Strategy with IFR of Coronary Artery Stenosis in Patients with Stable Coronary Artery Disease

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Abstract

Background: Stable coronary artery disease (CAD) presents with intermediate lesions that complicate treatment decisions. Visual assessment of coronary angiography may not accurately reflect the hemodynamic significance of these lesions. Instantaneous Wave-Free Ratio (IFR) is a new physiological index providing objective information on lesion functional significance. **This study aimed to** detect magnitude and direction of reclassification of intermediate lesions treatment after hemodynamic assessment by IFR in patients with stable CAD. **Methods:** This prospective observational study was carried out on 50 patients with stable coronary artery disease admitted to a single center. Patient received coronary angiography for a consultant's visual evaluation in order to identify the first treatment protocol. Hemodynamic assessment using IFR was performed for intermediate lesions to reclassify the treatment strategy. **Results**: The mean age of the patients was 64.2 ± 12.11 years, with 76% males and 24% females. The majority of patients had hypertension (74%), followed by diabetes mellitus (46%), hyperlipidemia (64%), smoking history (62%), and chronic kidney disease (22%). Based on the IFR assessment, 80% of patients were reclassified to receive medical treatment, while 20%

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underwent PCI. **Conclusion:** Our study results show that IFR is a reliable and accurate tool for guiding revascularization decisions in CAD patients. The majority of patients in our study, 80%, were safely reclassified to medical treatment based on IFR results. In the remaining 20% of patients, IFR results showed significant lesions that required PCI.

Keywords: Reclassification; Treatment Strategy; IFR; Coronary Artery Stenosis; CAD.

Introduction:

CAD continues to be one of the world's top causes of morbidity and death. It is characterized by the progressive narrowing of the coronary arteries due to the buildup of atherosclerotic plaques, leading to inadequate blood supply to the heart muscle. Stable coronary artery disease, a manifestation of CAD, is typically associated with chronic and stable symptoms, such as angina, and is managed through various treatment strategies [1].

The decision-making process regarding the optimal treatment strategy for stable CAD patients can be challenging, especially when faced with intermediate coronary artery lesions [2]. These lesions, with a degree of stenosis ranging from 40% to 70%, present a dilemma for clinicians as they often lack clear evidence of functional significance based on angiographic imaging alone. Consequently, there is a need for additional tools that can accurately assess the physiological impact of such lesions [3].

Hemodynamic assessment techniques, such as fractional flow reverse (FFR), have been widely adopted to assess the functional significance of coronary artery stenosis. FFR measures the pressure gradient across a stenosis during maximum hyperemia and has been shown to guide treatment decisions effectively. However, FFR requires the administration of potent vasodilators, which can be time-consuming, costly, and potentially related to complications [4].

In recent years, the emergence of IFR has offered a non-hyperemic alternative for assessing coronary artery stenosis. IFR leverages the concept of wave-free period, a specific time interval during the cardiac cycle where the pressure drop across a stenosis is independent of microvascular resistance. By utilizing this period, IFR provides an index that correlates well with FFR and can be measured without the need for pharmacological vasodilation [5].

Given the potential benefits of IFR, there is a growing interest in exploring its role in reclassifying treatment strategies for patients with stable CAD and intermediate lesions. This reclassification refers to the process of revising treatment decisions based on the additional information supplied by hemodynamic assessment [6]. By accurately

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identifying lesions that are functionally significant, IFR has the potential to guide clinicians towards more personalized and targeted interventions, optimizing patient outcomes while minimizing unnecessary invasive procedures [7].

This study aimed to investigate the extent and direction of treatment reclassification in patients with stable CAD and intermediate lesions following hemodynamic assessment using IFR.

Patients and methods:

This prospective observational single center study was conducted on 50 patients with stable coronary artery disease of intermediate lesions admitted to coronary care unit at national heart institute during the period from January 2021 to January 2022. An informed written consent was obtained from all patients. The study was done after approval of ethical committee of Benha faculty of Medicine.

Study protocol: Patients with chronic stable CAD go for coronary angiography for visual assessment by consultant to determine mode of treatment either medical or PCI or CABG then hemodynamic assessment by IFR for intermediate lesions for reclassification of treatment according to IFR reading and consultant opinion either medical or PCI or CABG.

Inclusion criteria were Age > 18 years of age, eligible for coronary angiography and/or percutaneous coronary intervention and stable angina.

Exclusion criteria applied in this study were: individuals who had previously undergone coronary artery bypass grafting (CABG) with patent grafts to the specific vessel under investigation, individuals with significant narrowing of the left main coronary artery, individuals with tandem narrowings separated by less than 5mm that necessitated separate pressure guide wire assessment or percutaneous coronary intervention (PCI) (these were not considered as a single narrowing and were excluded), individuals with complete blockage of the coronary artery, individuals with restenosis lesions, individuals who were hemodynamically unstable at the time of the procedure (with a heart rate below 50 beats per minute or a systolic blood pressure below 90mmHg), individuals requiring a balloon pump, individuals with contraindications to PCI or the implantation of drug-eluting stents (DES), individuals with significant liver or lung disease (such as chronic obstructive pulmonary disease), individuals with malignant disease that had an unfavorable prognosis and could potentially impact survival within the next 5 years, pregnant individuals, individuals who experienced a ST-segment elevation myocardial infarction (STEMI) within 48 hours of the procedure, individuals

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with severe valvular heart disease, and individuals with acute coronary syndrome (ACS) who had more than one target vessel present.

All patients had medical history including full history taking, risk factors of CAD involving Family history, Cigarette smoking, Dyslipidemia, Hypertension, Diabetes mellitus and other comorbidities, prior history of intervention, drugs, time of presentation from the start of symptoms. Full clinical examination: general examination, local examination as well as auscultation of the back, auscultation of the heart and vital signs.

Laboratory investigations including hemoglobin, white blood cells, platelets, creatinine, Urea, Troponin I and CKMB: It is a creatine kinase isoenzyme. Creatine kinase converts creatine phosphate to creatine, therefore supplying the energy necessary for ATP regeneration [8].

Baseline echocardiography: All patients were assessed by echocardiography using Philips HP Sonos 5500. for the evaluation of regional wall anomalies and left ventricular systolic function as a whole, any valvular affection, mechanical complications, pulmonary hypertension, chamber dilatation.

Investigations: Base line electrocardiography: Electrocardiography was performed to all patients; the ECG was recorded simultaneously. To detect any abnormalities, for ST segment deviation either elevation or depression, T wave inversion, QRS and rhythm.

Pre-Angiography testing:

Procedure: Angiographic assessment: Visual assessment of lesion by consultant then hemodynamic assessment by IFR for intermediate lesions for reclassification of treatment either medical or PCI or CABG.

IFR: Invasive functional assessment: If the physiological relevance of one or more stenosis is uncertain, the patient was eligible for enrollment. Typically, coronary stenosis within the range of 40 to 70 percent will serve as a guideline. Upon intubation of the guiding catheter, 300mcg of intracoronary nitrates was administered followed by introducing of IFR wire, normalization followed by introducing of wire to the lesion and calculation of IFR then assessment using the official documented protocol of IFR assessment [9].

Post-PCI / Post-Angiography Testing: PCI intervention: PCI was done through the femoral and radial arteries using Seldinger`s technique for patients if the intervention is needed due to chronic coronary syndrome [10].

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Prior to IFR evaluation, treating interventionalists were required to choose one of three a priori angiogram-based therapeutic approaches, namely optimum medical therapy (OMT), percutaneous coronary intervention (PCI) of 1, 2, or 3 arteries, or coronary artery bypass grafting (CABG).

IFR/consultant measurements dictated the ultimate treatment selection, which was likewise grouped according to these 5 options. Before intracoronary physiological testing, intracoronary nitroglycerin was given. Utilizing a coronary pressure guidewire, measurements were collected (Philips Volcano, Rancho Cordova, California). According to current revascularization recommendations, an IFR of #0.89confirmed the presence of a hemodynamically significant lesion requiring revascularization through PCI or CABG.

Statistical analysis

SPSS v26 was used to do statistical analysis (IBM Inc., Armonk, NY, USA). Using the Shapiro-Wilks test and histograms, the normality of the data distribution was determined. As mean and standard deviation (SD), quantitative parametric data were given. Non-parametric quantitative data are provided as the median and interquartile range (IQR). The qualitative data were presented as a frequency and percentage distribution (%). Cohen's Kappa is a quantitative measure of reliability for two raters. A two tailed P value < 0.05 was considered statistically significant.

Results:

Demographic data and risk factors of the studied patients: The study was performed on 50 patients. the mean age was 64.2 ± 12.11, 37 patients were hypertensive, 23 patients were diabetic, 32 patients were hyperlipidemic.

Examination and clinical data: The mean HR were 83.3 ± 9.22 beats/min. The mean SBP was 135.2 ± 9.74 mmHg. The mean DBP was 76.2 ± 9.67 mmHg. The mean O_2 saturation was 97 ± 1.53. The mean RR was 19.8 ± 1.49 breaths/min. **Laboratory data:** The mean Hb was 11.1 ± 1.03 g/dL. The mean WBCs was 8 ± 1.88 $x10^3$/L. The mean creatinine was 0.9 ± 0.4 mg/dL. The mean urea was 47.8 ± 22.19 mg/dL.The mean troponin was 0.1 ± 0.13 ng/ml, The mean CK-MB was 0 ± 0.01 ng/ml

Echocardiographic data: The mean LVEF was 59.5 ± 3.28 %. The mean E/E' was 9.1 ± 0.87. The mean SV was 64.1 ± 3.13 ml. The mean LV mass was 147.8 ± 43.02. The mean LVESD was 30.4 ± 5.06. The mean LVEDD was 47.5 ± 5.16 mm. The mean LVMI was 78.5 ± 20.11 g/m²

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Angiographic results: 28 (56%) patients had LAD, 9 (18%) patients had RCA, 7(14%) patients had LAD & LCX, 4 (8%) patients had LAD & RCA, 2 (4%) patients had LAD & 1st OM. **Figure 1**

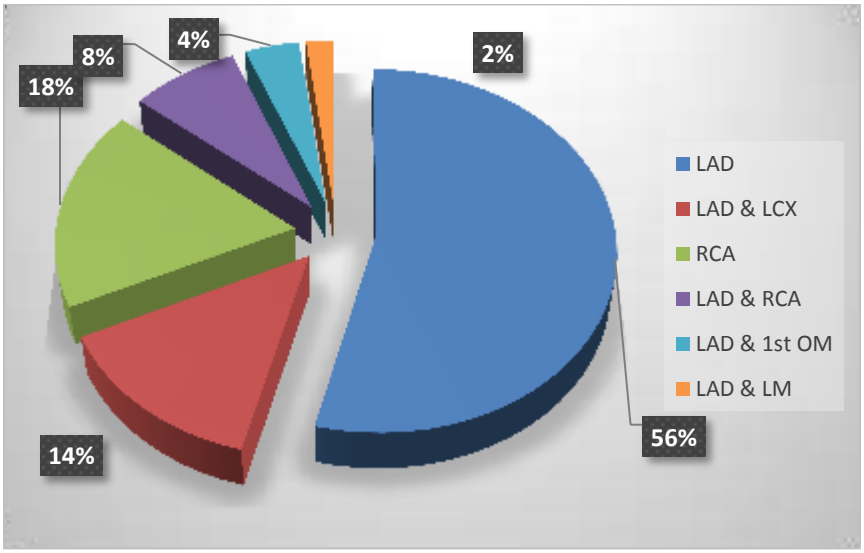

Figure 1: Lesion types of the studied patients

LAD presented in 28 patients, 26 patients according to IFR showed non-significant lesion, so reclassified to medical treatment. While in two patients, IFR results showed significant lesion so converted from medical treatment to PCI. RCA presented in 9 patients, 6 patients according to IFR showed non-significant lesion, so reclassified to medical treatment. While, in three patients, IFR results showed significant lesion, so PCI was done. LAD & LCX presented in 7 patients, 6 patients according to IFR showed non-significant lesion, so reclassified to medical treatment. While, in one patient, IFR results showed significant lesion, so PCI was done. LAD & OM presented in 2 patients, 2 OM patients according to IFR showed non-significant lesion, so reclassified to medical treatment. LAD in one patient, IFR results showed significant lesion, so PCI was done. LAD in one patient, IFR results showed significant lesion, so converted from medical treatment to PCI. LAD & RCA presented in 4 patients, RCA according to IFR showed non-significant lesion, so reclassified to medical treatment. While LAD, IFR results showed significant lesion, so PCI was done. LAD presented in 2 patients, RCA according to IFR showed non-significant lesion, so reclassified to medical treatment. While one patient, IFR results showed non-significant lesion, so medical treatment. **Table 1**

Table 1: IFR results

	IFR result	
	Non-significant	**Significant**
LAD	26	2
RCA	6	3

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LAD & LCX		6	1
LAD & OM	**LAD**	-	2
	OM	2	-
LAD & RCA	**LAD**	2	2
	RCA	4	-

LAD: left anterior descending artery, RCA: right coronary artery, OM: obtuse marginal, LCX: left circumflex artery, LM: left main

Regarding reclassification, 80% had medical treatment, 20% had PCI.

Discussion:

Instantaneous Wave-Free Ratio (IFR) has emerged as a promising non-hyperemic index for the functional assessment of coronary artery stenosis. IFR leverages the concept of a wave-free period during the cardiac cycle, where the pressure drop across a stenosis is independent of microvascular resistance. This technique enables the assessment of the functional significance of intermediate lesions without the need for pharmacological vasodilators, addressing the limitations associated with traditional approaches [11].

The utility of IFR in the reclassification of treatment strategies for patients with stable CAD and intermediate lesions is of significant clinical interest. By providing additional functional information about the lesions, IFR has the potential to refine treatment decisions, avoiding unnecessary invasive procedures for lesions that are not functionally significant while ensuring appropriate interventions for those that are [12].

This study aimed to investigate the magnitude and direction of reclassification of treatment strategies in patients with stable CAD and intermediate lesions after hemodynamic assessment using IFR.

In terms of baseline characteristics and in agreement with the current study, a study reported similar patients' characteristics to the current work [13].

In the present work, 28 (54%) patients had LAD, 9 (18%) patients had RCA, 7(14%) patients had LAD & LCX, 4 (8%) patients had LAD & RCA, 2 (4%) patients had LAD & 1st OM. The majority of patients had a lesion in the LAD artery, followed by RCA and LAD & LCX. These findings are consistent with the results of other studies. A study found that the LAD artery was the most commonly affected vessel in patients with coronary artery disease, followed by RCA and LCX [14].

Regarding our findings, LAD presented in 28 patients, 26 patients according to IFR showed non-significant lesion, so reclassified to medical treatment. While in two patient, IFR results showed significant lesion, so converted from medical treatment to PCI.

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Regarding the current work, RCA presented in 9 patients, 6 patients according to IFR showed non-significant lesion, so reclassified to medical treatment. While, in three patients, IFR results showed significant lesion, so PCI was done.

The study provided information on coronary artery involvement occurrence in patient population and the subsequent management based on both the invasive functional assessment using IFR and consultant opinion. The results of this study are consistent with previous research that demonstrated the efficacy of invasive functional assessment in reclassifying patients for management decisions. A study showed that reclassifying patients using IFR caused a reduction in patients number undergoing PCI without compromising clinical outcomes [15].

Furthermore, the results of the present study demonstrated that in some cases, there was a discrepancy between the consultant's opinion and IFR results in determining the significance of the lesion. This finding is consistent with a previous study that showed that there was a moderate level of agreement between consultant opinion and FFR results in determining the need for revascularization [16].

Regarding reclassification, 80% had medical treatment, 20% had PCI.

The study results show that in most cases, patients with LAD lesions were reclassified to medical treatment based on IFR, with only two patients being converted from medical treatment to PCI based on IFR results. This finding is consistent with a previous study which found that using IFR in patients with intermediate coronary stenosis resulted in a significant reduction in unnecessary revascularization procedures [13].

Regarding reclassification, the study found that 80% of patients were reclassified to medical treatment, while only 20% underwent PCI. This finding is similar to previous studies which found that using IFR in patients with intermediate coronary stenosis resulted in a significant reduction in the number of patients undergoing PCI [7,17].

In summary, the study results suggest that IFR can be an effective tool for guiding treatment decisions in patients with intermediate coronary stenosis and can help reduce unnecessary revascularization procedures.

The use of physiological assessments such as IFR to guide treatment decisions for intermediate coronary artery stenosis is a topic of ongoing research. Our study showed that IFR can be an effective tool in reclassifying treatment strategies for patients with stable coronary artery disease. Our findings are consistent with previous studies that have demonstrated the clinical utility of IFR in guiding treatment decisions for intermediate lesions.

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A study showed that among patients with intermediate coronary artery stenosis, Those who received IFR-guided therapy had a considerably reduced incidence of major adverse cardiac events than those who received angiography-guided therapy [12].

Similarly, a meta-analysis found that IFR-guided therapy was related to a decreased risk of major adverse cardiac events and a lower rate of unnecessary revascularization compared to angiography-guided treatment [18].

Our study also supports the findings of a recent study, which showed that among patients with stable angina and intermediate coronary artery stenosis, those who underwent IFR-guided treatment had a lower rate of major adverse cardiac events and a higher rate of deferral of revascularization compared to those who underwent angiography-guided treatment [19].

Finally, this study had some limitations: the study had a relatively small sample size, the follow-up period was limited to short period, IFR not available in all angiographic centers, also the study did not compare with gold standard. Therefore, future multi-center studies should overcome these limitations.

Conclusion:

The results of our study demonstrate that IFR is a reliable and accurate tool for guiding revascularization decisions in patients with CAD. The majority of patients in our study, 80%, were safely reclassified to medical treatment based on IFR results. In the remaining 20% of patients, IFR results showed significant lesions that required PCI. This study reveals the benefits of using IFR in clinical practice to assess the decision-making process in patients with CAD. IFR is an attractive alternative to traditional invasive methods, such as FFR, for assessing the severity of coronary artery lesions.

Conflicts of interest

No conflicts of interest

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