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Original article

Role of Instantaneous Wave-Free Ratio in Detection of Residual Significant Ischemia after Successful Angiographic Percutaneous Coronary Intervention

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Abstract:

Background: Despite angiographic success after percutaneous coronary intervention (PCI), a substantial proportion of cases experience residual ischemia (RI), contributing to adverse outcomes. Instantaneous wave-free ratio (iFR) offers a practical, vasodilator-free method to assess post-PCI functional results. This study aimed to estimate the prevalence, predictors, and clinical implications of RI (iFR ≤ 0.89) following angiographically successful PCI. **Methods:** This prospective investigation encompassed 100 hemodynamically stable coronary artery disease (CAD) cases who underwent angiographically successful PCI. Post-PCI iFR was measured. Cases were stratified by iFR into RI (≤ 0.89) (n=28) and non-ischemic (> 0.89) (n=62) groups. Clinical and angiographic characteristics were compared. One-year MACEs were tracked. **Results:** RI was detected in 28% of cases. These cases were significantly older (67 ± 10 vs. 61 ± 9 years, P = 0.009), had elevated BMI (30 ± 4 vs. 28 ± 3 kg/m², P = 0.024), and more CKD (35.7% vs. 12.5%, P = 0.012). They also had more severe stenosis (79 ± 5% vs. 68 ± 7%, P < 0.001), longer lesions (28 mm vs. 17 mm, P < 0.001), and more calcifications (60.7% vs. 37.5%, P = 0.036). Kaplan-Meier analysis showed substantially higher 1-year MACE in the ischemic group (16.6% vs. 0%, log-rank P < 0.001; HR = 38.14, 95% CI: 10.01–145.39). **Conclusion:** RI post-angiographically successful PCI is not uncommon and is associated with specific clinical and lesion-related predictors and worse clinical outcomes. Post-PCI iFR assessment may uncover functionally suboptimal results that merit further optimization.

Keywords: Percutaneous Coronary Intervention; Instantaneous Wave-Free Ratio; Residual Ischemia; MACE.

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Introduction

Since the advent of coronary angioplasty, substantial progress has been achieved in minimizing postprocedural ischemic complications, including in-stent restenosis and stent thrombosis. Advances in stent engineering and in pharmacological therapy have substantially lowered the rate of acute vessel closure from approximately 8% to under 1%, while the incidence of target vessel revascularization has declined from nearly 30% to around 5%. Despite these developments, stent-related complications still contribute substantially to morbidity [(1)].

Intravascular imaging modalities like intravascular ultrasound (IVUS) and optical coherence tomography (OCT) have revealed that many stents are suboptimally deployed despite appearing successful on angiography. These modalities can detect issues such as incomplete expansion, malposition, edge dissection, or inadequate lesion coverage, all of which have been linked to adverse outcomes. However, intracoronary imaging remains underutilized in routine clinical practice due to additional costs, technical challenges in complex anatomy, and the need for operator expertise in image interpretation [(2, 3)].

In contrast, coronary physiological assessment using indices such as wave-free ratio (iFR) and FFR offers a more practical approach in many clinical settings. iFR, in particular, allows for the functional evaluation of coronary lesions without the use of pharmacologic vasodilation, thus avoiding side effects associated with adenosine used in FFR. It also employs smaller, more deliverable catheters, making it feasible even in calcified or tortuous vessels [(4)].

The use of pressure-derived indices has demonstrated clear prognostic value when used before percutaneous coronary intervention (PCI) in patients with stable ischemic heart disease (SIHD), and the 2024 ESC guidelines recommend using pressure flow measurements before and after PCI to guide treatment and improve outcomes [(5)].

The iFR is a pressure-based metric assessed during the diastolic wave-free period, a phase characterized by inherently low and stable microvascular resistance. It is determined by calculating the ratio of distal to proximal coronary pressure (Pd/Pa) averaged over five cardiac cycles, and notably, its measurement does not necessitate the induction of pharmacologic hyperemia [(6)]. Its simplicity and reproducibility offer a promising tool for assessing the functional success of PCI and detecting residual ischemia (RI) not evident angiographically [(7)].

The purpose of this investigation is to evaluate the prevalence of residual significant ischemia using iFR after angiographically successful PCI and to explore its predictive value for clinical outcomes, as well as to identify procedural and anatomical factors contributing to suboptimal physiological results.

Patients and methods:

This prospective, non-randomized study was conducted during the period from January 2023 to January 2024 at Benha University Hospitals and the National Heart Institute. A total of 100 cases with hemodynamically stable CAD who underwent angiographically successful PCI were enrolled.

Informed written consent was secured from all participants after thoroughly explaining the study's aims. To maintain confidentiality, each patient was allocated a unique code number. The research commenced only after obtaining formal ethical approval from the Faculty of Medicine's Research Ethics Committee at Benha University (Approval number: MD 21-12-2022).

Inclusion criteria were adults aged 18 years or older with stable CAD and angiographic lesions of ≥40% severity. While, exclusion criteria encompassed recent STEMI, cardiogenic shock,

arrhythmias, prior CABG, severe LV dysfunction (EF <30%), chronic total occlusions, and patient refusal.

All cases underwent comprehensive clinical evaluation, including detailed history. Physical examination included general and cardiovascular assessment, anthropometric measurements, and vital signs. Routine laboratory investigations, standard 12-lead ECG, and transthoracic echocardiography using Simpson's biplane method were also performed to assess cardiac rhythm and LVEF.

Coronary Angiography and PCI Protocol:

All cases underwent coronary angiography followed by PCI using standard techniques. DES were deployed following lesion preparation. Intracoronary nitroglycerin (100–200 μg) was administered prior to pressure wire measurements. Lesions were assessed for location (LAD, LCX, RCA, LM), type, length, severity, calcification, branch involvement, and bifurcation [(8)].

Physiological Assessment Using iFR:

iFR measurements were obtained using the Verratta™ pressure wire and Volcano system. Readings were taken at least three vessel diameters distal to the lesion and normalized at the coronary ostium. Pre-PCI and post-stenting iFR were recorded. An iFR ≤ 0.89 post-stenting indicated RI, prompting further intervention or optimization. Cases were then divided into group 1: iFR ≤ 0.89 (with RI) and group 2: iFR > 0.89 (no RI). Final iFR was recorded post-optimization.

Lesion and Procedural Characteristics:

Data included lesion segment (proximal/mid/distal), lesion classification (types A/B/C), lesion severity (% diameter stenosis), number of stents, stent diameter and length, calcification, in-stent restenosis, and multivessel disease.

Follow-Up and Clinical Outcomes:

All cases were followed up for 12 months through clinic visits and telephone contact. Major endpoints included recurrence of angina, myocardial infarction, cardiovascular death, stroke, and need for repeat revascularization. Composite MACE was calculated at 1-year.

Sample size:

Sample size was calculated using Epi Info™ with 99.9% CI, 80% power, and a previously reported RI prevalence of 30% [(7)]. A total of 100 cases were recruited using consecutive non-probability sampling.

Statistical analysis

Statistical analysis was performed using SPSS version 27 (IBM, Armonk, NY, USA). The Shapiro-Wilk test assessed the normality of quantitative data, which were expressed as mean ± SD or median and range based on distribution. Categorical data were summarized as counts and percentages. Group comparisons utilized the independent t-test or Mann–Whitney U test, within-group differences were analyzed with the paired t-test, and categorical variables were compared using the chi-square or Fisher's exact test. ROC analysis evaluated the predictive value of final iFR for composite MACE. Logistic regression identified MACE predictors, and Kaplan-Meier analysis estimated MACE occurrence over time. Significance was defined as a *p*-value less than 0.05.

Results:

General characteristics between studied groups

Cases with impaired post-PCI iFR (≤ 0.89) were significantly older (67 ± 10 vs. 61 ± 9 years, P = 0.009) and had elevated BMI (30 ± 4 vs. 28 ± 3 kg/m², P = 0.024) relative to those with normal iFR. They also showed a substantially higher prevalence of CKD (35.7% vs. 12.5%, $P = 0.012$). Although males were more represented in the impaired group, the variation was not statistically significant ($P = 0.182$). No substantial variations were found regarding diabetes ($P = 0.084$), HTN ($P = 0.076$), smoking ($P = 0.404$), dyslipidemia ($P = 0.095$), prior MI ($P = 0.191$), prior PCI ($P = 0.533$), family

history of CAD ($P = 0.948$), or EF ($P = 0.178$). (**Table 1)**

Lesion characteristics between the studied groups

Cases with impaired post-PCI iFR (≤ 0.89) exhibited a markedly elevated mean percentage of stenosis (79 ± 5% vs. 68 ± 7%, $P < 0.001$) and longer lesion length (28 mm [15–50] vs. 17 mm [12–34], $P < 0.001$) compared to those with normal iFR. Multiple lesions were more frequent in the impaired group (64.3% vs. 22.2%, $P < 0.001$), while single lesions predominated in the normal group (77.8% vs. 35.7%). The impaired group also had lower pre-dilatation iFR (0.68 ± 0.08 vs. 0.78 ± 0.05, P < 0.001) and more calcified lesions (60.7% vs. 37.5%, $P = 0.036$). LAD artery was more commonly affected in the impaired group (64.3% vs. 33.3%, $P = 0.022$), with proximal lesions being significantly more frequent (64.3% vs. 29.2%, $P = 0.005$). Lesion morphology also differed, with type A lesions more common in the normal group (36.1% vs. 7.1%) and type B/C lesions dominating in the impaired group (92.9% vs. 63.9%, $P = 0.004$). No substantial variations were noted in rates of multivessel disease ($P = 0.056$) or in-stent restenosis ($P = 0.182$). (**Table 2)**

Procedural characteristics between the studied groups

Cases with impaired post-PCI iFR (≤ 0.89) required significantly more extensive stenting, with a higher rate of two-stent use (35.7% vs. 13.9%, $P = 0.021$) and longer total stent lengths (33 mm vs. 18 mm, $P < 0.001$). Other procedural parameters, such as pre-dilatation, stent diameter, and post-dilatation, showed no significant differences. (**Table 3)**

1-Year clinical events according to final IFR

At one-year follow-up, cases with impaired final iFR (≤ 0.89) had a markedly higher incidence of cardiovascular death (15.4% vs. 1.1%, $P = 0.044$), myocardial infarction (23.1% vs. 2.3%, $P = 0.015$), and revascularization (23.1% vs. 5.7%, $P = 0.032$) compared to those with final iFR > 0.89. Additionally, the composite rate of MACE was significantly higher in impaired iFR group (61.5% vs. 9.2%, $P < 0.001$). (**Figure 1)**

Final iFR between cases with and without composite MACE

Cases who developed composite MACE at one year had a significantly lower mean final iFR compared to those without MACE (0.89 ± 0.06 vs. 0.95 ± 0.03, $P = 0.001$).

ROC analysis of final IFR to predict composite MACE occurrence

ROC curve analysis was done for final iFR to predict the occurrence of composite MACE. It revealed a significant AUC of 0.785 with a 95% CI ranging from 0.622 to 0.948, suggesting a very good ability to predict composite MACE. The best cutoff point was ≤ 0.9, at which the sensitivity, specificity, PPV, and NPV were 75%, 89.29%, 57.1%, and 94.9%, respectively. (**Figure 2)**

Kaplan Meier analysis for composite MACE occurrence

Kaplan-Meier analysis showed a progressive increase in composite MACE over time, reaching 16.6% at 12 months. Cases with RI (final iFR ≤ 0.89) had a substantially higher MACE incidence relative to those without, with a log-rank $P < 0.001$ and an adjusted HR of 38.14 (95% CI: 10.01–145.39). (**Figure 3)**

Prediction of residual ischemia (iFR ≤ 0.89)

All variables showed statistical significance < 0.1 were included in a univariate logistic regression analysis, followed by a stepwise multivariate analysis. The multivariate analysis revealed that dyslipidemia was independently associated with a higher risk of RI (OR = 4.825, 95% CI: 1.034–22.521, $P = 0.045$). Proximal segment affection showed a strong predictive value, with a 41.65-fold increased risk of RI (OR = 41.65, 95% CI: 4.12–419.248, $P = 0.002$). Each 1% increase in stenosis severity was associated with a 36.1% increased risk

(OR = 1.361, 95% CI: 1.142–1.621, P < 0.001). Moreover, larger stent diameter significantly reduced the risk of RI (OR = 0.044, 95% CI: 0.003–0.622, *P* = 0.021). (**Table 4)**

Table 1: General characteristics between the studied groups

		iFR ≤ 0.89		Total	
		No (n = 62)	**Yes (n = 28)**		**P-value**
Age (years)	Mean ±SD	61 ±9	67 ±10	63 ±9	**0.009***
Gender					
Males	n (%)	41 (56.9)	20 (71.4)	61 (61)	0.182
Females	n (%)	31 (43.1)	8 (28.6)	39 (39)	
BMI (kg/m²)	Mean ±SD	28 ±3	30 ±4	29 ±3	**0.024***
DM	n (%)	25 (34.7)	15 (53.6)	40 (40)	0.084
HTN	n (%)	46 (63.9)	23 (82.1)	69 (69)	0.076
Smoking	n (%)	22 (30.6)	11 (39.3)	33 (33)	0.404
Dyslipidemia	n (%)	41 (56.9)	21 (75)	62 (62)	0.095
FH of PCAD	n (%)	15 (20.8)	6 (21.4)	21 (21)	0.948
CKD	n (%)	9 (12.5)	10 (35.7)	19 (19)	**0.012***
Prior MI	n (%)	21 (29.2)	12 (42.9)	33 (33)	0.191
Prior PCI	n (%)	26 (36.1)	12 (42.9)	38 (38)	0.533
EF (%)	Mean ±SD	57 ±10	54 ±9	56 ±10	0.178

n: number, BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, FH of PCAD: Family history of premature coronary artery disease, CKD: Chronic kidney disease, MI: Myocardial infarction, PCI: Percutaneous coronary intervention, EF: Ejection fraction, SD: Standard deviation, *: Significant P-value.

Table 2: Lesion characteristics between the studied groups

		iFR ≤ 0.89		Total	
		No (n = 62)	**Yes (n = 28)**		**P-value**
Culprit vessel					
LAD	n (%)	24 (33.3)	18 (64.3)	43 (43)	**0.022***
RCA	n (%)	28 (38.9)	4 (14.3)	36 (36)	
LCX	n (%)	18 (25)	5 (17.9)	18 (18)	
LM	n (%)	2 (2.8)	1 (3.6)	3 (3)	
Segment affected					
Proximal	n (%)	21 (29.2)	18 (64.3)	33 (33)	**0.005***
Mid	n (%)	31 (43.1)	6 (21.4)	48 (48)	
Distal	n (%)	20 (27.8)	4 (14.3)	19 (19)	
% Stenosis	Mean ±SD	68 ±7	79 ±5	71 ±8	**<0.001***
Lesion length (mm)	Median (range)	17 (12 - 34)	28 (15 - 50)	19 (12 - 50)	**<0.001***
Lesion number					
One	n (%)	56 (77.8)	10 (35.7)	66 (66)	**<0.001***
Two	n (%)	16 (22.2)	18 (64.3)	34 (34)	
iFR predilatation	Mean ±SD	0.78 ±0.05	0.68 ±0.08	0.75 ±0.08	**<0.001***
Calcification	n (%)	27 (37.5)	17 (60.7)	44 (44)	**0.036***
Lesion type					
A	n (%)	26 (36.1)	2 (7.1)	28 (28)	**0.004***
B & C	n (%)	46 (63.9)	26 (92.9)	44 (44)	
MVD	n (%)	26 (36.1)	16 (57.1)	28 (28)	0.056
ISR	n (%)	7 (9.7)	6 (21.4)	42 (42)	0.182

n: number, LAD: Left anterior descending artery, RCA: Right coronary artery, LCX: Left circumflex artery, LM: Left main coronary artery, iFR: Instantaneous wave-free ratio, MVD: Multivessel disease, ISR: In-stent restenosis, SD: Standard deviation, *: Significant P-value.

Table 3: Procedural characteristics between the studied groups

		iFR ≤ 0.89			P-value
		No (n = 62)	Yes (n = 28)		
Pre-dilatation	n (%)	28 (38.9)	16 (57.1)	44 (44)	0.099
Number of stents					
One	n (%)	61 (84.7)	17 (60.7)	78 (78)	
Two	n (%)	10 (13.9)	10 (35.7)	20 (20)	**0.021***
Three	n (%)	1 (1.4)	1 (3.6)	2 (2)	
Total stent length (mm)	Median (range)	18 (15 - 36)	33 (18 - 64)	22 (15 - 64)	**<0.001***
Stent diameter (mm)	Mean ±SD	3.11 ±0.46	2.91 ±0.48	3.06 ±0.47	0.058
Post dilatation	n (%)	31 (43.1)	16 (57.1)	47 (47)	0.205

n: number, iFR: Instantaneous wave-free ratio, SD: Standard deviation, *: Significant P-value.

Table 4: Logistic regression analyses to predict residual ischemia (iFR ≤ 0.89)

	Univariate		Multivariate	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
Age (years)	1.069 (1.015 - 1.126)	**0.012***	-	-
BMI (kg/m²)	1.197 (1.041 - 1.376)	**0.012***	-	-
DM	2.169 (0.893 - 5.267)	0.087	-	-
HTN	2.600 (0.883 - 7.657)	0.083	-	-
Dyslipidemia	2.268 (0.856 - 6.010)	0.099	4.825 (1.034 -22.521)	**0.045***
CKD	3.889 (1.372 - 11.022)	**0.011***	-	-
LAD affection	3.6 (1.442 - 8.99)	**0.006***	-	-
Proximal segment affection	4.371 (1.733 - 11.025)	**0.002***	41. 65 (4.12 -419.248)	**0.002***
% Stenosis	1.392 (1.207 - 1.606)	**<0.001***	1.361 (1.142 - 1.621)	**<0.001***
Lesion length (mm)	1.155 (1.082 - 1.232)	**<0.001***	-	-
Two lesions	6.300 (2.432 - 16.322)	**<0.001***	-	-
Calcification	2.576 (1.051 - 6.310)	**0.038***	-	-
Lesion type (B & C)	7.348 (1.613 - 33.478)	**0.01***	-	-
MVD	2.359 (0.969 - 5.742)	0.059	-	-
Pre-dilatation	2.095 (0.864 - 5.081)	0.102	-	-
Number of stents			-	-
One	R	R	-	-
Two	3.588 (1.283 - 10.033)	**0.015***	-	-
Three	3.588 (0.213 - 60.407)	0.375	-	-
Total stent length (mm)	1.156 (1.084 - 1.233)	**<0.001***	-	-
Stent diameter (mm)	0.376 (0.135 - 1.047)	0.061	0.044 (0.003 - 0.622)	**0.021***

OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, CKD: Chronic kidney disease, % Stenosis: Percent stenosis, MVD: Multivessel disease, iFR: Instantaneous wave-free ratio, *: Significant P-value.

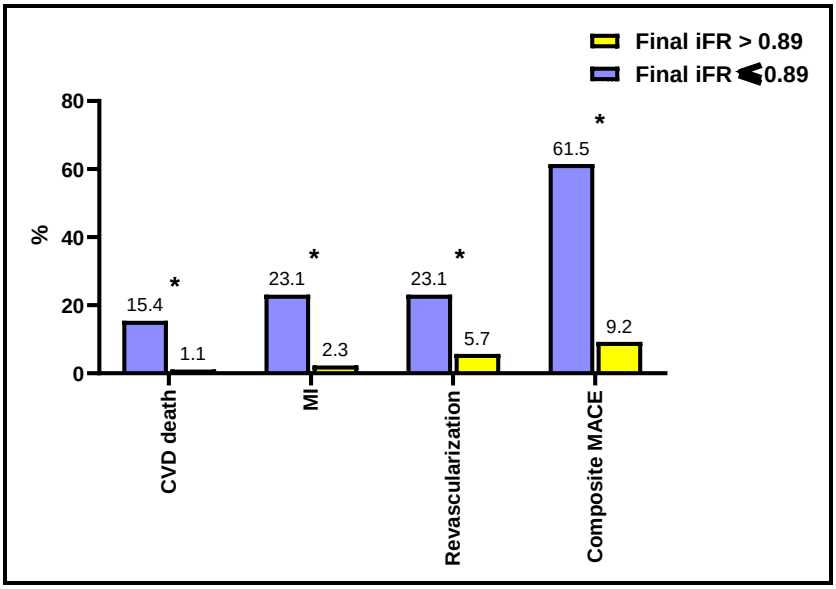

Figure 1: 1-Year clinical events according to final IFR

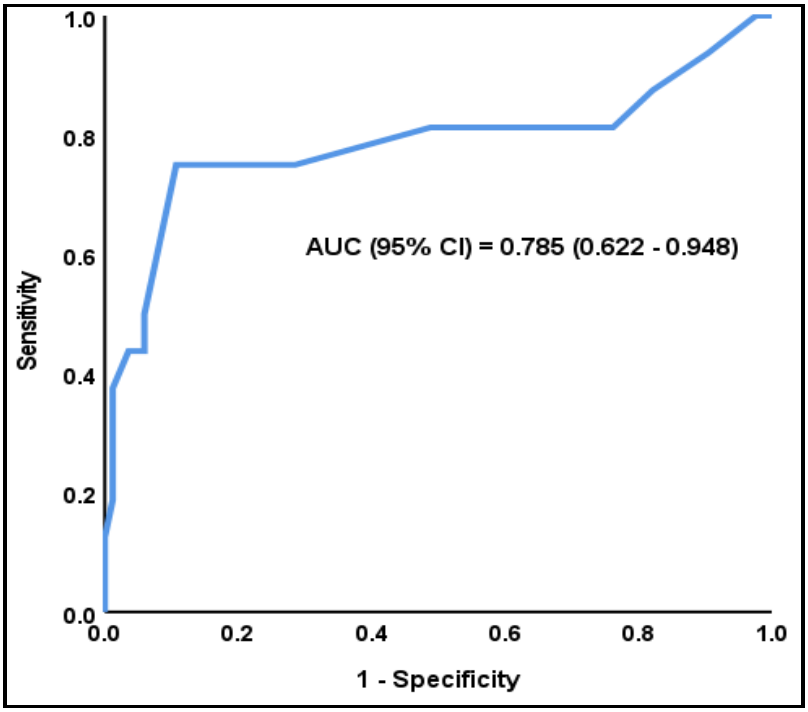

Figure 2: ROC analysis of final IFR to predict composite MACE occurrence

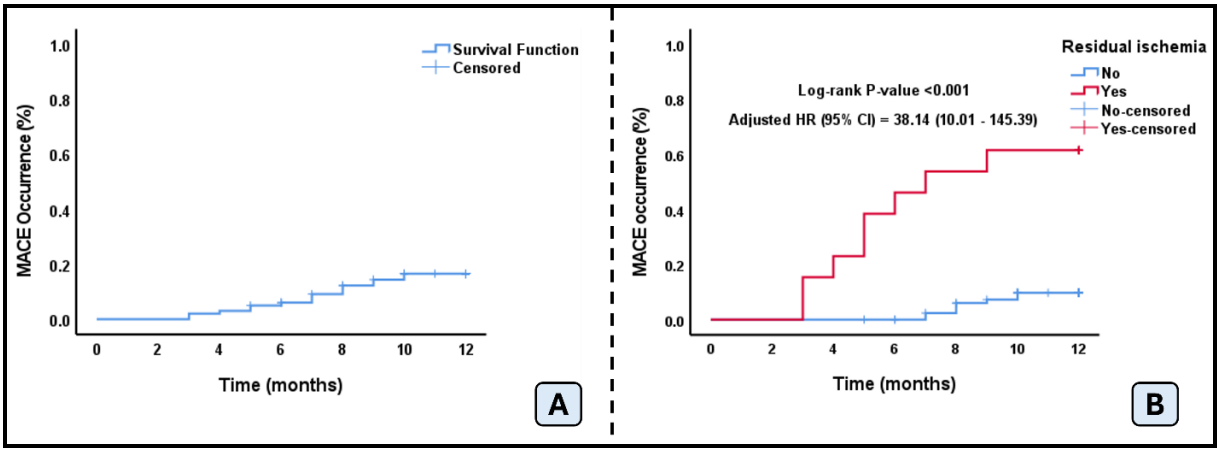

Figure 3: Kaplan Meier analysis for composite MACE occurrence in the studied patients (A) and according to final IFR (B)

Discussion:

Even after a visually perfect angioplasty, the heart may still be starved of blood. Therefore, this study explores the hidden ischemia detected by iFR after a successful PCI—aiming to identify its predictors and impact on outcomes.

Our study demonstrated a significant improvement in iFR values following stent deployment, indicating effective relief of coronary obstruction. Among all patients, the mean iFR significantly increased after stent deployment (P < 0.001). Then the patients were categorized based on post-stenting iFR values into two groups: those with RI (28 patients) and those without RI (72 patients). Among patients with impaired post-PCI iFR, the predominant cause was stent-related issues such as under-sizing or under-expansion, accounting for 57.1% of cases. Missed culprit lesions were identified in 25%, while diffuse coronary disease was the cause in 17.9%. as identified by iFR pull back at end of procedure.

This goes in harmony with Jeremias et al.[9] study in which RI post angiographically successful PCI as detected by post PCI IFR was 24%, with 81% untreated focal lesions, 38% of them inside the stent and 18% were diffuse lesion, also study assumed that this 24% with RI could be reduced to 4.9% by further optimization. In Wolfrum et al. [10] in which suboptimal functional results after conventional stenting defined as FFR<90% were noticed in 60% of patients, two third of them were inside the the stent. But this large number could be attributed to the lesions involved in the study were all complex lesions only. In contrast to Pijls et al. [11] that all involved lesions were simple not complex lesion, impaired post PCI FFR were detected in 6% only of patients also cut off point for impaired FFR was <0.8. In Kasula et al. [12] RI post PCI as detected by post PCI FFR<0.8 were detected in 21% of patients. In Uretsky et al. [13] RI post PCI as detected by post PCI FFR<0.8 were detected in 36.5% of patients. In Neleman et al. [14] in which FFR guided optimization using IVUS vs standard of care, RI was detected in 23% of patients defined by FFR <0.8, of those impaired FFR group, the cause in 62% was inside the stent and 16% distal to stent and 14% proximal to stent and 8% were diffuse CAD.

Regarding general characteristics between study groups, Patients with impaired iFR group were significantly older, had higher BMI, and a greater prevalence of chronic kidney disease (CKD), this is explained by in older patients & in patients with CKD have more microvascular dysfunction, more diffuse and calcific CAD. Other

clinical characteristics such as diabetes, hypertension, smoking, and prior cardiac history revealed no significant differences between the two groups. Consistent with our findings, Kovach et al. [15] investigated the association between residual ischemic burden and long-term clinical outcomes in a large cohort of 57,476 U.S. veterans undergoing PCI. Patients in the highest tertile of residual disease were significantly older (67.9 ± 9.6 years) and had a higher prevalence of CKD (25.7%) compared to those with complete revascularization (17.3%) ($P < 0.001$ for both). However, unlike our study, they found an inverse trend in BMI across residual disease tertiles, possibly due to differences in population demographics and the chronicity of disease. And In alignment with our findings, Abtan et al. [16] examined residual ischemic risk over a 4-year period in 16,770 patients with prior myocardial infarction. They found a steady increase in ischemic events, from 4.7% in year one to 15.1% by year four, highlighting the persistent burden of RI despite contemporary therapy. Risk factors associated with recurrent events included older age—consistent with the adverse clinical profile observed in our patients with impaired post-PCI iFR (≤0.89), who were also older.

Regarding lesion characteristics in the current study, patients with impaired post-PCI iFR (≤ 0.89) tended to had a significantly more complex coronary lesions, including higher degrees of stenosis, longer lesion lengths, more frequent multiple (as defined by Poiseuille law of fluid dynamics the gradient across coronary stenosis in inversely proportional to the fourth power of the lesion radius and proportional to lesion length).In harmony with this is, Wong et al. [17] that developed score incorporating lesion lengths & degrees of stenosis that shows incremental predictive value in detecting significant stenosis **,** the same for, Hoole et al. [18] that developed FAST score for prediction of lesion significance depending on lesion length and diameter stenosis that was highly discriminative & predictive (95% confidence interval, $p<0.0001$). The pre-dilatation iFR was significantly lower in the impaired group ($P < 0.001$). This goes with, Uretsky et al. [13] in which lower pre-PCI FFR correlates significantly with impaired post PCI FFR, $p<0.0001$). Lesion morphology varied significantly, with type A lesions more frequent in the normal iFR group, and type B and C lesions dominating in the impaired group ($P = 0.004$). with significant predominance of and calcified lesions in impaired group. As in Uretsky et al. [13] in which lesion calcification correlates significantly with post PCI FFR, $p<0.0001$. Natsumeda et al. [14] that showed that tendem lesion types B&C are significantly associated with impaired post PCI FFR, $p<0.0001$.

Culprit vessel distribution showed a significant difference, with LAD lesions more prevalent in the impaired group. Lesion location also differed significantly, with proximal-segment lesions being more frequent in the impaired group ($P = 0.005$) (both LAD & proximal position supply large myocardial territory, higher flow rate and have higher shear stress favors plaque formation). Similarly, Matsumura et al. [19] they noted a substantially lower ΔiFR in LAD vessels (0.09) compared to non-LAD vessels (0.26, $p < 0.0001$), and a higher prevalence of post-PCI iFR ≤ 0.89 in LAD cases (30.9% vs. 6.7%, $p < 0.0001$) emphasizing that RI remains prevalent despite angiographic success, particularly in LAD lesions, and that iFR can uncover functional inadequacies—especially when in-stent focal disease persists.

Regarding procedural characteristics between the studied groups, Patients with impaired post-PCI iFR (≤ 0.89) required significantly more stents, with single-stent use being less frequent compared to those with normal iFR, while the use of two stents was higher. Additionally, the total stent length was significantly greater in the impaired group. This goes with Uretsky et al. [13] in which longer stent length &

multiple rather than single use of sttents were associated with impaired post PCI FFR. Also the same in Kawase et al. [20] that showed longer total stent length, stent diameter correlates significantly with impaired post PCI FFR**.**

Other procedural parameters, including impaired post-PCI iFR (≤ 0.89) required more pre-dilatation (P = 0.099), (as lesions of impaired post PCI FFR tend to be more complex the need proper lesion preparation by pre-dilatation and proper stent expansion and apposition by post-dilatation), lower stent diameter (P = 0.058), and more post-dilatation (P = 0.205), but did not significantly differ between groups.This is in harmony with Wolfrum et al [10] study that measured post PCI suboptimal FFR results and optimized them using OCT, revealed that group with impaired post PCI FFR need more pre-dilatation and more post-dilatation and significantly lower stent dimeter.

In response to suboptimal post-PCI iFR, additional post-dilatation was performed in 57.1% of affected cases, and further stenting was required in 17.9%. These interventions led to an improvement in the mean final post-PCI iFR. Despite optimization efforts, 13% of patients had a final iFR ≤ 0.89, while 87% achieved a final iFR > 0.89. In our study patients with RI (iFR ≤ 0.89) who underwent further intervention, a subsequent significant increase in mean iFR was observed from 0.82 after post-dilatation to 0.91 following final post-PCI optimization (P < 0.001), and all patients had significant increase in mean iFR was observed from 0.91 ± 0.06 after post-dilatation to 0.93 ± 0.04 following final post-PCI optimization (P < 0.001). In Neleman et al. [14] trial, further optimization by additional stenting in 16%, additional post dilatation in 33.6%, no additional treatment in 31%, both dilatation and stenting in 18%, this improved post PCI FFR in this group from 0.82 to 0.89 p<0.0001. In Kasula et al. [12] RI detected in 21% of patients have been reduced to 9.5% by further intervention (42% additional post dilatation, 33% additional stenting, 18% both stenting and dilatation). In Burzotta et al. [21] study, both post PCI FFR & OCT performed in all patients post PCI, they revealed 14.5% mal-apposition, 7.6% under-expansion, 2.7% edge dissection, further optimization improved FFR in 25% of patients, 81% additional post dilatation & 12% additional stenting with improved mean FFR from 0.86 to 0.90. In Wolfrum et al. [10] in which suboptimal functional results after conventional stenting defined as FFR<90% were found in 60% of patients, that have been reduced to 23% by further optimization (by additional stenting in 39%, additional post dilatation in 46%, both dilatation and stenting in 15%).

In our one-year follow-up analysis, patients with an impaired final iFR exhibited a significantly elevated incidence of cardiovascular mortality, myocardial infarction, and revascularization (P = 0.032) compared to those with final iFR > 0.89. Additionally, the composite rate of MACE was significantly higher in the impaired iFR group underscoring the prognostic importance of achieving optimal physiological results post-PCI. And patients who developed composite MACE at one year had a significantly lower mean final iFR compared to those without MACE.

In the present investigation at one-year follow-up, cases with impaired final iFR (≤ 0.89) experienced markedly worse clinical outcomes, including higher rates of cardiovascular death, MI, revascularization, and overall MACE. Furthermore, those who developed MACE had markedly lower final iFR values compared to those without events, underscoring the prognostic importance of achieving optimal physiological results post-PCI. Parallel to our findings, Patel et al.[22] in the DEFINE PCI trial, observed RI (iFR ≤0.89) in 24% of post-PCI cases, predominantly attributable to angiographically unapparent focal lesions.

Additionally, a post-PCI iFR ≥0.95 was associated with significantly redcued one-year event rates and greater angina relief, underscoring the clinical benefit of achieving higher physiological indices after intervention. Similarly, Griffioen et al.[23] found in a meta-analysis of 4,017 cases that impaired iFR (≤ 0.95) was independently associated with increased rates of MI and target vessel revascularization. Kovach et al.[15] also showed that a higher residual SYNTAX score (>7) was associated with elevated 1-year MACE. Lee et al.[24] demonstrated that lesions with low FFR (≤0.80) or iFR (≤0.89) were associated with significantly higher two-year rates of MACEs, especially when both indices were concordantly abnormal, emphasizing the prognostic value of physiological assessment. Nam et al.[25] reported that a post-PCI FFR below 0.90 was associated with a significantly higher one-year rate of MACEs compared to higher FFR values. Doh et al.[26] found that a post-PCI FFR less than 0.89 predicted target vessel failure at three years, with significantly higher incidence compared to cases with higher FFR values. The DK-CRUSH VII study by Li et al.[27] identified an FFR ≤0.88 as a threshold for poor prognosis following drug-eluting stent implantation, associated with higher rates of target vessel failure, revascularization, and cardiac death. Additionally, a meta-analysis by Rimac et al.[28], including 105 studies with 7,470 cases, demonstrated that a post-PCI FFR ≥0.90 was linked to a significantly lower risk of revascularization and MACE.

In the present study, ROC curve analysis demonstrated that final iFR was a strong predictor of composite MACE, with a cutoff of ≤0.9 offering the optimal balance of sensitivity and specificity, indicating that suboptimal post-PCI iFR values are associated with a greater risk of adverse cardiovascular events. Consistent with these findings, Warisawa et al.[29] showed that iFR has significant prognostic value in guiding revascularization decisions for left main coronary artery disease. In their deferred revascularization cohort, iFR achieved an AUC of 0.74 with an optimal cutoff of 0.88 for predicting MACE, and a sub-analysis focusing on cardiac death and left main-related myocardial infarction demonstrated an even higher AUC of 0.80, underscoring the strong predictive capacity of iFR for adverse outcomes. Additionally, Petraco et al.[30] evaluated 216 stenoses and reported a high diagnostic performance of iFR for coronary flow velocity reserve, with an AUC of 0.82, further reinforcing iFR's clinical utility.

In our study, Kaplan-Meier analysis demonstrated a steady increase in composite MACE incidence over 12 months, rising from 2% at three months to 16.6% at one year. Stratification by RI status revealed that cases with a final iFR ≤0.89 faced a significantly higher risk of MACE compared to those with higher iFR values. This relationship was further supported by a substantially elevated adjusted hazard ratio, underscoring the prognostic significance of achieving optimal physiological outcomes post-PCI. Consistently, Warisawa et al.[29] reported that the deferred group experienced a significantly higher incidence of composite MACE (28.4%) compared with the revascularized group (14.9%) over a median follow-up of 34 months. Additionally, cardiac death or left main-related myocardial infarction occurred in 8.1% of the deferred group but in none of the revascularized cases. These results highlight the prognostic relevance of RI detected by iFR and align with our observation that lower post-PCI iFR values are strongly associated with adverse outcomes.

This study was limited by its relatively small sample size and dual-center design, which may affect the generalizability of results. Additionally, longer-term outcomes beyond one year were not assessed.

Conclusion:

iFR provides a simple, safe, and effective method for assessing coronary lesion significance without pharmacologic hyperemia. When used after PCI, it can reveal RI undetected by angiography, helping to optimize interventions and improve outcomes. As coronary physiology understanding advances, iFR is expected to have an increasingly vital role in guiding revascularization strategies.

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