Instantaneous wave–free ratio (IFR) VS myocardial perfusion imaging by single photon emission tomography (MPI-SPECT) in assessment of significance of moderate coronary artery disease

Sameh Refat Allam
Cardiovascular medicine Department, Faculty of Medicine, Al Azhar University, Egypt

Mohamed Abdel Hady Abdel Rehiem
Cardiovascular medicine Department, Faculty of Medicine, Al Azhar University, Egypt

Ayman Al saied Sadek
Cardiovascular medicine Department, Faculty of Medicine, Al Azhar University, Egypt

Essam Gaber Mohamed Nosier
Cardiovascular medicine Department, Faculty of Medicine, Al Azhar University, Egypt,
essamnoseir11@gmail.com

How to Cite This Article

ORIGINAL ARTICLE

Instantaneous Wave-free Ratio Versus Myocardial Perfusion Imaging by Single Photon Emission Tomography in Assessment of Significance of Moderate Coronary Artery Disease

Sameh R. Allam, Mohamed A.H.A. Rehiem, Ayman A.S. Sadek, Essam G.M. Nosier*

Cardiovascular Medicine Department, Faculty of Medicine, Al Azhar University, Cairo, Egypt

Abstract

Background: The noninvasive technique known as myocardial perfusion imaging (MPI) is used to assess the functional relevance of borderline coronary artery abnormalities. Additionally, a well-validated intrusive technique known as the instantaneous wave-free ratio (IFR) is employed for the same objective.

Aim and objectives: To compare perfusion imaging by single photon emission tomography (SPECT) as one of the commonly used noninvasive tests in the assessment of myocardial ischemia and instantaneous wave-free ratio as one of the new invasive tools in the evaluation of the significance of moderate coronary artery disease (CAD) lesion.

Patients and techniques: This is prospective research, conducted on 50 studied cases who were diagnosed as ischemic heart disease and admitted to the National Heart Institute and Al-Azhar University hospitals. Those patients were subjected to coronary angiography that showed moderate lesion (angiographically) in a single vessel then patients who had IFR results between 0.8 and 0.9 were scheduled for MPI SPECT to assess the significance of this border line lesion within 2 weeks of coronary angiography.

Result: There were 22 (44%) with positive IFR and the mean value of IFR was 0.88 ($\pm$0.08 SD) with range (0.75−1.04).

Conclusion: Both MPI SPECT and IFR found great sensitivity (90.9%), specificity (96.4%), negative predictive value (NPV) (93.1%), and pulse pressure variation (PPV) (95.2). So, the IFR can be a valid alternative to fractional flow reserve (FFR) to evaluate the functional significance of intermediate coronary lesions without using agents to induce maximal hyperemia.

Keywords: Coronary artery lesion, Instantaneous wave-free ratio, Myocardial perfusion imaging

1. Introduction

The syndrome of coronary artery disease (CAD) includes numerous clinical manifestations. According to onset and persistence of symptoms, variations in biochemical indicators, impact on left ventricular function, and a better understanding of underlying pathology, the classification of various clinical entities that make up CAD varies.

Coronary angiography in acute coronary syndrome (ACS) patients can classify studied cases that can gain from coronary revascularization.[1]

When compared with quantitative coronary angiography, physician visual assessment of stenosis yielded greater readings of stenosis severity, according to research published in February 2018 that examined coronary artery lesions treated with PCI in China. Research has also shown considerable differences between hospitals and doctors, supporting the value of further diagnostic tests.[2]

IFR is more recent physiologic measurement that employs concepts similar to those of fractional flow reserve (FFR) but does not call for administration of hyperemic drug. IFR and FFR showed no discernible variations in the prediction of myocardial ischemia in 2017 journal of American College of Cardiology research.[3] IFR-guided revascularization was noninferior to FFR-guided revascularization for

major adverse cardiac events at one year follow-up, according to MACE trial, which further supported its usage.[4]

FFR testing, meanwhile, is seen as very pricey procedure, especially given the limited resources in our nation. It necessitates the use of pharmacological hyperemic drugs like adenosine, which are not always readily available here. With our limited resources, the complication has been partially solved by the advancement of the Instantaneous wave-free ratio (IFR), a relatively new invasive technique for the physiological assessment of coronary lesions without the use of pharmacologic hyperemic agents. However, the test is still regarded as being relatively expensive.

Goal of our study was to compare perfusion imaging SPECT as a one of the commonly used noninvasive test in assessment of myocardial ischemia and instantaneous wave-free ratio as one of the new invasive tools in evaluation of significance of moderate CAD lesion.

2. Patients and methods

This was prospective research curried out at National Heart Institute and Al-Azhar university hospitals. The study population comprised 50 patients who diagnosed as ischemic heart disease and admitted to National Heart Institute and Al-Azhar university hospitals, during the study period, who were fulfilling the inclusion criteria.

2.1. Inclusion criteria

Studied cases with angiographically borderline coronary artery stenosis (47%) in single coronary artery and ischemic heart disease patients with IFR result between 0.9 and 0.8.

2.2. Coronary angiography

Coronary angiography was performed, and patients proved to have angiographically moderate lesion (40–70%) stenosis were evaluated by IFR those whose IFR results fall in gray zone (0.9–0.8) patient were scheduled for MPI SPECT within 2 weeks outcomes of MPI and IFR of each patient had been compared with each other.

2.3. Administrative considerations

The Faculty of Medicine at Al Azhar University granted official clearance.

2.4. Ethical consideration

Research has been approved by the Ethics Committee. All studied cases gave their informed consent after being made aware of research's objectives and methodology.

2.5. Data analysis

Using SPSS version 20, data entry, processing, and statistical analysis were completed (USA Statistical Package for Social Sciences). The Kruskal-Wallis, Wilcoxon, χ^2, logistic regression analysis, and Spearman's correlation tests of significance were applied. Depending on type of data (parametric and nonparametric) collected for each variable, data had been presented, and appropriate analysis was carried out. P values of 0.05 or lower (5%) were regarded as statistically significant.

3. Results

This prospective study was conducted on 50 patients who were diagnosed as ischemic heart disease and admitted to National Heart Institute and Al-Azhar university hospitals. Coronary angiography showed moderate lesion angiographically (40–70%) in a single vessel and IFR result was between 0.9 : 0.8 (gray zone). These patients were scheduled to MPI SPECT to assess the significance of this border line lesion within 2 weeks of coronary angiography. As regard distribution of the studied cases according to stenosis and target vessel, the present study revealed that there were 12 (24%) with left circumflex artery (LCX) as target vessel, 29 (58%) LAD and 9 (18%) right coronary artery RCA and that mean Percentage of stenosis was 60.5 (±7.58 SD) with range (50–70).

The present study showed that Creatine kinase-MB (CK-MB) was in the normal range. There were 19 (38%) out of range in FBG and HbA1C, this is because among the included patients there were 19 (38%) had DM. As regard, distribution of the studied cases according to MPI, the present study revealed that there were 21 (42%) with positive MPI and the mean defect size was 16.24 (±3.69 SD) with range (10–22).

As regard, distribution of the studied cases according to IFR, the present study revealed that there were 22 (44%) with positive IFR and the mean value of IFR was 0.88 (±0.08 SD) with range (0.75–1.04). The present study showed that MPI and IFR showed strong substantial agreement with kappa (κ) 0.878.

The present study we performed receiver operating characteristic (Roc) curve analysis for the use of MPI to predict IFR, and we found that using MPI

it was shown that it can predict IFR results with area under the curve (AUC) of 0.937, level of sensitivity 90.9%, specificity 96.4%, pulse pressure variation (PPV) 95.2%, negative predictive value (NPV) 93.1% and accuracy 94% (Tables 1–5).

Table 1. Distribution of the studied cases according to stenosis and target vessel.

	Cases (n = 50)
	No. (%)
The target vessel	
LCX	12 (24.0)
LAD	29 (58.0)
RCA	9 (18.0)
Percentage of stenosis	
Range	40.0–70.0
Mean ± SD	60.5 ± 7.58

There were 12 (24%) with LCX as target vessel, 29 (58%) LAD and 9 (18%) RCA and that mean Percentage of stenosis was 60.5 (±7.58 SD) with range (50–70).

Table 2. Distribution of the studied cases according to myocardial perfusion imaging.

	Cases (n = 50)
Defect size	
Range	10.0–22.0
Mean ± SD	16.24 ± 3.69
Results	No. (%)
Negative	29 (58.0)
Positive	21 (42.0)

Among the 50 patients studied 21 (42%) have positive MPI, myocardial perfusion imaging and the mean defect size was 16.24 (±3.69 SD) with range (10–22).

Table 3. Distribution of the studied cases according to instantaneous wave-free ratio.

	Cases (n = 50)
Value	
Range	0.8–0.9
Mean ± SD	0.88 ± 0.08
Results	No. (%)
Negative	28 (56.0)
Positive	22 (44.0)

There were 22 (44%) with positive IFR, instantaneous wave-free ratio and the mean value of IFR was 0.88 (±0.08 SD) with range (0.75–1.04).

Table 4. Agreement between myocardial perfusion imaging and instantaneous wave-free ratio.

	IFR		Kappa (κ)
	Positive no. (%)	Negative no. (%)	
MPI			
Positive	20 (40.0)	1 (2.0)	0.878
Negative	2 (4.0)	27 (54.0)	

MPI, myocardial perfusion imaging and IFR, instantaneous wave-free ratio showed strong substantial agreement with kappa (κ) 0.878.

Table 5. Receiver operating characteristic curve analysis for the use of myocardial perfusion imaging to predict instantaneous wave-free ratio.

	AUC	Sens%	Spec%	PPV%	NPV%	Accuracy %
MPI	0.937	90.9	96.4	95.2	93.1	94.0

Using MPI, myocardial perfusion imaging it was shown that it can validate IFR, instantaneous wave-free ratio results with AUC, area under the curve of 0.937, level of sensitivity 90.9%, specificity 96.4%, PPV 95.2%, NPV 93.1% and accuracy 94%.

4. Discussion

Single-photon emission tomography myocardial perfusion imaging has been utilized for long time to identify reversible ischemia; measure defect sizes and support therapeutic intervention decisions. Even early validation of invasive physiological evaluation by FFR is done using it. FFR is now regarded as gold standard test for this reason even though that studied case result research on role of invasive physiological evaluation by FFR produced prestigious position and illuminated hot spot on its use.[5]

Their were no previous studies were found in literature compared MPI and IFR, however several studies were found have compared both MPI and IFR versus the standard FFR method. The meta-analysis by Zhou et al.,[6] aimed to determine effectiveness of myocardial perfusion SPECT to identify functionally stenotic CAD using fractional flow reserve as gold standard. 1017 studied cases from thirteen articles were included in research.

However, meta-analysis by Maini et al.,[7] with addition of 8 more current research and 3727 additional lesions, sought to offer appropriate update of diagnostic accuracy of IFR linked to FFR. Meta-analysis enrolled 16 studies comprising 5756 lesions. As regard distribution of the studied cases according to stenosis and target vessel. Our study was comparable to the reported results by Amin et al.,[5] as they revealed that there were 10 (20%) with LCX as target vessel, 32 (64%) LAD and 8 (16%) RCA.

As well, Zayed,[8] reported that left anterior descending artery was target vessel in 23 (38.3%) patients. Left circumflex artery was the target vessel in 20 (33.3%) patients. RCA was the target vessel in 17 (28.3%) patients.

Also, Matsushita et al.,[9] reported that there were 10 (12.5) with LCX as target vessel, 47 (58.8) LAD and 23 (28.8) RCA. However, research by Amin et al.,[5] described that 30 (60%) of studied patients had been positive MPI and the mean defect size was 15.6 ± 4.5 with range (10–22). However, study by Amin et al.,[5] described that 20 (40%) of studied patients had been positive IFR and the mean defect size was 0.89 ± 0.094 with range (0.65–1.05).

Our study was supported by Amin et al.,[5] who reported that total agreement was 96% and IFR and

FFR data showed strong (kappa = 0.918) significant (P < value 0.001) agreement. Additionally, there was 88% overall agreement and strong (kappa = 0.754) significant (P value < 0.001) agreement among IFR and FFR data.

Also, our results were supported by Zayed,[8] who reported that 6 studied cases were included; 37 (61.7%) had significant IFR values, while t23 (38.3%) had insignificant IFR values. Thirty-one (81.1%) of the 37 studied cases with substantial IFR values had positive MPI findings, while seven (18.9%) had negative outcomes. Nineteen (82.6%) of the 23 studied cases with negligible IFR values had negative outcomes, whereas 4 (17.4%) had positive outcomes. Findings of MPI and IFR were in good (kappa = 0.62), substantial (P = 0.001) agreement.

Also, study by Safi et al.,[10] reported that regarding detection of ischemia in implicated LAD region (kappa = 0.565, P < 0.001), LCX territory (kappa = 0.815, P 0.001), and RCA territory (kappa = 0.776, P < 0.001), there had been significant concordance among FFR and MPI with SPECT methods.

Our study was supported by Amin et al.,[5] who revealed that IFR had negative likelihood ratio of 0.09, negative predictive value of 93.3%, positive predictive value of 100%, specificity of 100%, sensitivity of 90.9%, and specificity of one hundred percent. Additionally, MPI's specificity, sensitivity, positive predictive value, negative predictive value, positive likelihood ratio, positive likelihood ratio, positive likelihood ratio, and negative likelihood ratio all stood at 81.8, 92.9, 90, 86.7%, 0.20 and 11.45, respectively.

Also, Zayed,[8] reported that MPI had been found to have great overall sensitivity and specificity (81.1 and 82.6%, respectively). Moreover, it showed high PPV and NPV (88.2 and 73.1%, respectively), and the accuracy was 81.7%. Erhard et al.[11] who concluded that SPECT-MPI was carried out and sensitivity and specificity were 83% and 77%, respectively, when used to evaluate the results of FFR. Another study evaluated 40 patients using the pressure wire during coronary angiography and compared results with MPI using thallium-201, and research determined that FFR can accurately assess occurrence of ischemia on SPECT in studied cases with stable CAD.[12]

Moreover, Sahiner et al.[13] showed that MPI-SPECT had overall sensitivity and specificity of 85 and 84%, and it had been more accurate than visual analysis.

Moreover, other study showed MPI-SPECT overall sensitivity and specificity had been 73 and 83%, respectively, with positive and negative likelihood ratios were 4.2 and 0.3.[14] Sensitivity and specificity of MPI had been 76 and 38%. PPV and NPV of MPI had been 66 and 50%, respectively, compared with FFR.[15] Moreover, Zhou et al.[6] indicated that multivessel and left main disease were a major obstacle to MPI in evaluation of functional significance of coronary artery lesion.

4.1. Conclusion

There was significant agreement between IFR approach and SPECT for MPI. Both MPI SPECT and IFR displayed great sensitivity, specificity, NPV, and PPV in this situation. As result, IFR, rather than fractional flow reserve, could be reliable option for determining functional relevance of intermediate coronary lesions without need for drugs that cause maximal hyperemia.

Consent for publication

Not applicable.

Availability of data and materials

Data and materials were available.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Conflicts of interest

The authors declared that there were no conflicts of interest.

References

1. Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the task force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32:2999—3054 [PubMed] [Google Scholar].
2. Zhang H, Mu L, Hu S, et al. China PEACE Collaborative Group. Comparison of physician visual assessment with quantitative coronary angiography in assessment of stenosis severity in China. *JAMA Intern Med*. 2018 Feb 01;178(2): 239—247.

3. Hwang D, Jeon KH, Lee JM, et al. Diagnostic performance of resting and hyperemic invasive physiological indices to define myocardial ischemia: validation with 13N-ammonia positron emission tomography. *JACC Cardiovasc Interv*. 2017 Apr 24;10(8):751−760.

4. Götberg M, Christiansen EH, Gudmundsdottir IJ, et al. iFR-SWEDEHEART Investigators. Instantaneous wave-free ratio versus fractional flow reserve to guide PCI. *N Engl J Med*. 2017 May 11;376(19):1813−1823.

5. Amin OA, Hady YA, Esmail MA. Myocardial perfusion imaging by single-photon emission tomography (MPI SPECT) versus Instantaneous wave-free ratio (IFR) for assessment of functional significance of intermediate coronary artery lesions. *Egypt Heart J*. 2019 Dec;71(1):35.

6. Zhou T, Yang LF, Zhai JL, et al. SPECT myocardial perfusion versus fractional flow reserve for evaluation of functional ischemia: a meta analysis. *Eur J Radiol*. 2014 Jun 1;83(6):951−956.

7. Maini R, Moscona J, Katigbak P, et al. Instantaneous wave-free ratio as an alternative to fractional flow reserve in assessment of moderate coronary stenoses: a meta-analysis of diagnostic accuracy studies. *Cardiovasc Revasc Med*. 2018 Jul 1; 19(5):613−620.

8. Zayed A. Invasive versus noninvasive assessment of functional significance of intermediate coronary artery lesions. *J Med Sci Res*. 2021 Jan 1;4(1):50.

9. Matsushita K, Hibi K, Okada K, et al. Comparison between instantaneous wave-free ratio versus morphometric assessments by intracoronary imaging. *Heart Ves*. 2019 Jun;34(6): 926−935.

10. Safi M, Karimlu MR, Khaheshi I, Ataeinia B. Concordance between myocardial perfusion scan assessed by SPECT and fractional flow reserve findings for detection of significant ischemia. *Egypt Heart J*. 2016 Sep 1;68(3):193−195.

11. Erhard I, Rieber J, Jung P, et al. The validation of fractional flow reserve in patients with coronary multivessel disease: a comparison with SPECT and contrast-enhanced dobutamine stress echocardiography. *Z Kardiol*. 2005;94:321−327. Back to cited text no. 15.

12. Caymaz O, Fak A, Tezcan H, et al. Correlation of myocardial fractional flow reserve with thallium-201 SPECT imaging in intermediate-severity coronary artery lesions. *J Invasive Cardiol*. 2000;12:345−350. Back to cited text no. 16.

13. Sahiner I, Akdemir UO, Kocaman SA, Sahinarslan A, Timurkaynak T, Unlu M. Quantitative evaluation improves specificity of myocardial perfusion SPECT in the assessment of functionally significant intermediate coronary artery stenoses: a comparative study with fractional flow reserve measurements. *Ann Nucl Med*. 2013;27:132−139. Back to cited text no. 17.

14. Knuuti J, Ballo H, Juarez-Orozco LE, et al. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a metaanalysis focused on post-test disease probability. *Eur Heart J*. 2018;39: 3322−3330. Back to cited text no. 20.

15. Melikian N, De Bondt P, Tonino P, et al. Fractional flow reserve and myocardial perfusion imaging in patients with angiographic multivessel coronary artery disease. *JACC Cardiovasc Interv*. 2010;3:307−314.