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Assessment of the Efficacy and Safety of the Instantaneous Wave-Free Ratio in a Real-World Setting

Research Article

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Clarissa Campo Dall'Orto*, Rubens Pierry Ferreira Lopes, Gilvan Vilella Pinto Filho and Marcos-Raphael da Silva

Department of Hemodynamic and Interventional Cardiology, Brazilian Society of Health Support Hospital, Brazil

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***Corresponding author:** Clarissa Campo Dall'Orto, Department of Hemodynamic and Interventional Cardiology, Brazilian Society of Health Support Hospital, Av. Pres. Getúlio Vargas - Recanto do Lago, 2752, Teixeira de Freitas, Bahia, 45987-088, Brazil

Abstract

Background:The limitations of visual angiographic assessment in coronary artery disease are well known. When intermediate lesions are submitted for functional assessment, there is a reclassification in the initial therapeutic decision in up to 33% of patients. Additional diagnostic modalities have been developed, such as the instantaneous wave-free ratio (iFR) evaluation, to characterize these patients with intermediate lesions better.

Methods: This prospective single-center study investigated the prognosis of intermediate coronary stenoses assessed by the iFR. Consecutive patients from January 2017 to January 2020, whose iFR was assessed in our hospital and had one or more moderate coronary lesions were included. Patients were divided into Group A (deferred lesions [65 patients with 93 assessed lesions]) and Group B (revascularized lesions [25 patients with 37 lesions]).

Results :There was no difference in demographic characteristics and clinical symptoms at presentation between the groups. The radial artery approach was performed in both groups, with crossover rates of the arterial access of 4.61% in Group A and 4% in Group B, although this was not statistically different. The volume of contrast used ($p = 0.001$) and fluoroscopy time ($p = 0.05$) were higher in Group B than in Group A. The average duration of late follow-up was 390.1 + 289.1 days, with no significant difference between the groups ($p = 0.202$). The variables associated with the need for new urgent revascularization and death (cardiac and non-cardiac) were not different between the groups ($p = 0.689$ and $p > 0.999$, respectively). There was no case of infarction in either group.

Conclusion: Our study showed the safety of the iFR-based invasive physiology method in patients deferred from coronary revascularization in daily clinical practice. Both groups of patients had low rates of adverse cardiac events and death at the late follow-up.

What is Known:

• Fractional flow reserve evaluation is the gold standard diagnostic modality to measure the pressure gradient between the chosen lesion and the aortic root.

• The instantaneous wave-free ratio uses principles similar to that of the fractional flow reserve but does not require adenosine.

What the Study Adds:

• The instantaneous wave-free ratio is a safe and effective diagnostic measure in a real-world setting.

• Both patients deferred and those recommended for revascularization showed low rates of adverse cardiac events and death using the instantaneous wave-free ratio as an indicator.

Introduction

The limitations of visual angiographic assessment in coronary artery disease (CAD) are well known. In addition to having inter- and intraobserver discrepancies, it can also not predict the hemodynamic impact of coronary stenosis [1-3]. When intermediate lesions are submitted for functional assessment, there is a reclassification in the initial therapeutic decision in up to 33% of patients [4,5].

More recently, we have seen the advent of the instantaneous wave-free ratio (iFR), whose principle is similar to that of fractional flow reserve (FFR) but without the need for a hyperemia-inducing agent. Instead, the pressure gradient calculation through the lesion is measured by software during the "wave-free period" of diastole, where there is lower and more stable vascular resistance. The SWEDEHEART [6] and DEFINE-FLAIR [7] studies showed that among patients with stable angina or ACS, the iFR-guided revascularization strategy was not inferior to that guided by FFR in the rate of major adverse cardiac events in 12 months.

In the present study, our purposes were to evaluate the efficacy of the iFR as a diagnostic modality in terms of major adverse cardiac events and to determine if the benefits of randomized controlled trials (RCTs) in iFR-guided coronary revascularization can also be achieved in the real-world setting.

Methods

Study design: The present study was a prospective single-center registry designed to investigate the prognosis of intermediate coronary stenoses assessed by iFR. The registry included all consecutive patients with one or more moderate coronary lesions evaluated by iFR in our service from January 2017 to January 2020. If positive for ischemia by the iFR, patients were referred for myocardial revascularization, either by open surgery (CBAG) or coronary angioplasty (PCI), depending on the clinical condition and the heart team decision. Thus, 90 patients were divided into groups according to myocardial revascularization performance after the invasive physiology method.

The study was approved by the Research Ethics Committee of the Federal University of the South of Bahia and the participants signed the consent form. The study was registered on the Brazilian government's website that legislates research, Plataforma Brasil (https://plataformabrasil.saude.gov.br).

Inclusion criteria: All patients > 18 years of age with CAD, be it acute coronary syndrome (ACS) or stable angina, whose angiographic lesion was 40%–80% stenotic on visual analysis of coronary angiography and who underwent the invasive coronary physiology assessment procedure, were included.

Exclusion criteria: Patients who were pregnant or those with hemodynamic instability at the time of the intervention (heart rate <50 beats per minute or systolic blood pressure <90 mmHg); coronary lesions with a flow <2 by the classification thrombolysis in myocardial infarction (TIMI); contraindications for percutaneous coronary intervention or drug-eluting stent implantation; patients with concomitant severe heart valve disease; or patients with a malignant disease with poor prognosis and life expectancy of <1 year were excluded.

Criteria for decision making by the operator: For patients who met the inclusion criteria, the operators followed the flow chart shown in Figure 1. The iFR was calculated for lesions in the coronary arteries with 40%–80% stenosis. If the iFR value was >0.93, the patient was not designated for revascularization (Group A) and remained under optimal clinical treatment (deferred lesions). If the iFR value was <0.86, the patient was referred for revascularization (Group B). When the value of the iFR was in the range of 0.86 to 0.93, FFR was also performed. Since the iFR is a relatively new technology, some studies considered values in the range of 0.86 to 0.93 to be located in an area of uncertainty and recommended taking a hybrid approach with FFR [8-10].

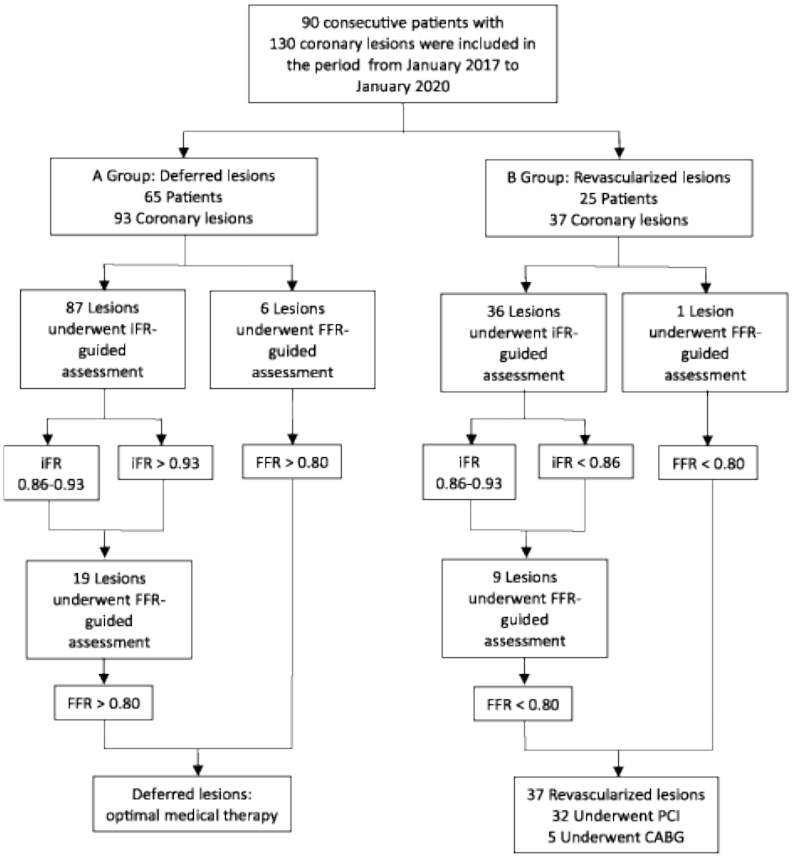

Figure 1: Enrollment and lesion treatment strategies.

In the latter case, if the FFR was >0.80, the patient was not referred for revascularization (Group A) and underwent optimized clinical treatment (deferred lesions). If the FFR was <0.80, the patient was referred for revascularization, belonging to Group B. All revascularization procedures were performed using current standard techniques. In the case of PCI, all patients received second-generation drug-eluting stents and double antiplatelet therapy.

FFR realization protocol: FFR was measured by placing the Verrata® coronary guide wire (Philips Volcano, Rancho Cordova, CA, USA) with a pressure transducer at its distal end through the coronary lesion. The patients received intracoronary nitroglycerin administration and full heparinization before passing the guide wire through the coronary artery. Adenosine was then administered to assess the pressure gradient across the lesion during maximum hyperemia. The FFR value resulted from the pressure ratio through the lesion during maximum hyperemia and pressure in the aorta.

iFR realization protocol: The iFR is a physiological index used to assess the severity of angiographic strictures. It was calculated by measuring the pressure gradient at rest through the coronary lesion during diastole with low and stable microvascular resistance. The benefits of iFR include obtaining an instant evaluation of the lesion without administering an agent to cause reactive hyperemia. The patients received intracoronary nitroglycerin and full heparinization before passing the guide wire through the coronary artery. Like FFR, IFR was also measured by placing a guide wire with a pressure transducer at its distal end through the coronary lesion. We used the same Verrata® guide wire (Philips Volcano).

Study outcomes and follow-up: Patients were followed up by telephone contact at 1, 3, 6, and 12 months after the procedure, and annually thereafter. In case of any doubt about an outcome and/or information referred by the patient, a face-to-face consultation was requested. In these telephones and/or face-to-face contacts, the presence of the following outcomes was assessed: death,

MI, and the need for new urgent revascularization. All deaths were considered cardiac unless their non-cardiac origin could be clearly established by clinical study and/or medical records.

MI was defined a priori in the study protocol as the appearance of new pathological Q waves on the electrocardiography in at least two contiguous leads and/or an increase in high-sensitivity troponin >5 times the upper limit of normality during the index hospitalization. If troponin is not done or not available, then an increase in CK-MB >5 times the upper limit of normality will qualify.

The need for new urgent revascularization was defined as revascularization that was not part of the index procedure and was not identified during the index procedure as a procedure to be performed within the first 60 days after the procedure.

Statistical analysis: Continuous quantitative variables were assessed using the parametric Student's t-test. Numerical values are presented as the mean ± standard deviation. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. The latter was used when the sample number was <20 or >20 and <40, where the expected frequency was <5 cells. A binary logistic regression model was used to adjust the variables and assess differences between groups at the time of the event and in the outcomes. Statistical analyzes were performed using R software, version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria; URL: https://www.R-project.org/). P-values <0.05 were considered statistically significant.

Keywords: Coronary disease; Coronary stent; Fractional flow reserve; Revascularization

Results

Group A comprised 65 patients with 93 lesions evaluated. IFR was performed alone in 93 lesions and iFR followed by FFR in 19 lesions. Group B included 25 patients with 37 lesions evaluated. IFR was performed alone in 37 lesions and iFR followed by FFR in 8 lesions. (Table 1).

Table 1: Quantification of the sample studied in the different groups

Variable	Group A	Group B	General sample	p value
Patients – n (%)	65	25	90	-
Arteries assessed – n (%)	93	37	130	-
Total of lesions assessed by iFR – n (%)	93 (100)	37 (100)	130 (100)	0.522
Lesions assessed by iFR follow by FFR – n (%)	19 (20.4)	8 (2.7)	27 (20.7)	0.492

Table 2: Baseline clinical characteristics of the patients

Variable	Group A (N = 65)*	Group B (N = 25)*	General sample (N = 90)*	p value
Age – years	64.7 ± 11.8	64.6 ± 11.5	65.1 ± 11.9	0.962
Female sex – n (%)	24 (36.9)	13 (52)	32 (40)	0.410
Body-mass index†	26.7 ± 4.6	27.5 ± 3.08	26.6 ± 4.3	0.617
Creatinine clearance (mL/min)‡	91.6 ± 41.4	80.4 ± 44.6	87 ± 39.5	0.284
Hypertension – n (%)	59 (90.7)	25 (100)	74 (92.5)	0.772
Dyslipidemia – n (%)	49 (75.3)	21 (84)	61 (76.25)	0.758
Family history of coronary artery disease – n (%)	26 (40)	16 (64)	36 (45)	0.232
Former smoke – n (%)	14 (21.5)	8 (32)	20 (25)	0.428
Current smoke – n (%)	10 (15.3)	3 (12)	10 (12.5)	0.721
Diabetes mellitus – n (%)	22 (33.8)	12 (48)	27 (33.75)	0.414
Previous IM – n (%)	19 (29.2)	10 (40)	24 (30)	0.490
Previous PCI – n (%)	28 (43)	10 (40)	34 (42.5)	0.865
Previous CABG – n (%)	2 (3)	3 (12)	4 (5)	0.124
Previous stroke – n (%)	1 (1.5)	1 (4)	1 (1.2)	0.490
Peripheral vascular disease – n (%)	2 (3)	0 (0)	2 (2.5)	0.382
Chronic obstructive pulmonary disease – n (%)	2 (3)	1 (4)	3 (3.7)	0.832

Table 3: Initial clinical presentation

Variable	Group A (N = 65)*	Group B (N = 25)*	General sample (N = 90)*	p value
Atypical precordial pain/anginal equivalent – n (%)	14 (21.5)	2 (8)	16 (17.7)	0.349
Silent ischemia – n (%)	2 (3)	2 (8)	4 (4.4)	0.575
Stable angina – n (%)†				
CCS angina class I	2 (3)	2 (8)	4 (4.4)	0.575
CCS angina class II	5 (7.6)	4 (16)	9 (10)	0.442
CCS angina class III	12 (18.4)	4 (16)	16 (17.7)	>0.999
CCS angina class IV	2 (3)	1 (4)	3 (3.3)	0.829
Unstable angina – n (%)†				
GRACE 1-108	12 (18.4)	1 (4)	13 (14.4)	0.176
GRACE 109-140	3 (4.6)	3 (12)	6 (6.6)	0.353
GRACE 141-372	1 (1.5)	2 (8)	3 (3.3)	0.201
Non-ST segment elevation IM – n (%)†				
GRACE 1-108	3 (4.6)	2 (8)	5 (6.2)	0.620
GRACE 109-140	2 (3)	0 (0)	2 (1.2)	0.382
GRACE 141-372	1 (1.5)	0 (0)	1 (1.2)	0.536
ST-segment elevation IM after thrombolysis – n (%)	6 (9.2)	2 (8)	8 (8.8)	0.866

Group A: deferred lesions; Group B: revascularized lesions.

Demographic characteristics showed no difference between age (mean age 65.19 ± 11.95), female sex, and

the presence of risk factors (Table 2). Regarding clinical symptoms at presentation, there was no difference between anginal equivalent, stable angina, unstable angina, and STEMI. There was a tendency for atypical pain to be more prevalent in Group A than in Group B (Table 3).

Data are presented as mean ± standard deviation or number (percentage). There were no significant differences in baseline characteristics between the two groups.

IM: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting.

* Number of patients.

†The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡Creatinine clearance was estimated using the Cockroft and Gault formula.

Data are presented as mean + standard deviation or number (percentage). There were no significant differences between the two groups in the initial clinical presentation. CCS: Canadian Cardiovascular Society; GRACE: Global Registry of Acute Coronary Events Score (scores range from 0 to 372); IM: myocardial infarction.

* Number of patients.

†CCS: Canadian Cardiovascular Society functional classification system (classes range from I to IV).

Table 4: Procedural characteristics related to variables by the number of patients

Variable	A Group (N = 65)*	B Group (N = 25)*	General sample (N = 90)*	p value
Radial-artery approach – n (%)	58 (89)	17 (68)	68 (85)	0.453
Caliber of sheath – n (%)				
5F	4 (6.1)	1 (4)	3 (4)	0.702
6F	61 (93.8)	24 (96)	77 (96)	0.946
Crossover radial for femoral approach – n (%)	3 (4.6)	1 (4)	3 (3.7)	0.903
Volume of ionic contrast medium (mL)	144.6± 63.6	195.3 ± 62.9	153.4 ± 65.2	0.001
Fluoroscopy (min)	17.0 ± 7.0	23.2 ± 9.2	17.9 ± 7.6	0.05
Procedure time (min)	59.2 ± 36.9	78.8 ± 39.9	61.4 ± 38.6	0.06
Multivessel disease – n (%)†	48 (73.8)	20 (80)	68 (75.5)	0.859
Ejection fraction – n (%)				
≥55%	45 (69.2)	15 (60)	53 (66.2)	0.706
≥40% and <55%	8 (12.3)	2 (8)	8 (10)	0.566
≥30% and <40	6 (9.2)	3 (12)	9 (11.2)	0.724
<30%	1 (1.5)	1 (4)	2 (2.5)	0.490
Left ventriculography not performed	5 (7.7)	4 (16)	8 (10)	0.294

Group A: deferred lesions; Group B: revascularized lesions.

‡In patients with acute coronary syndrome, only non-culprit lesions were evaluated.

The technical characteristics are listed in (Table 4). In most cases, the radial artery approach was utilized; the crossover rates to the femoral-artery approach were 4.61% in Group A and 4% in Group B, with no statistical difference. The volume of contrast used (p = 0.001) and fluoroscopy time (p = 0.05) were higher in Group B than in Group A. The total procedure time tended to be more in Group B (p = 0.06) than in Group A. We observed that the last three variables resulted from revascularization being performed immediately after coronary physiology analysis, in the same procedure. When the variables were adjusted using the binary logistic regression model, the presence of revascularization remained an independent predictor of a greater volume of contrast (p = 0.04).

Data are presented as mean ± standard deviation or number (percentage).

mL: millimeter; Min: minute.

*Number of patients.

†Defined as the presence of >50% stenosis in an epicardial coronary.

The angiographic characteristics did not differ between groups (Table 5). The values of iFR and FFR were lower in Group B than in Group A. In an average of 30% of the cases, there was a change in the operator's initial plan in both groups, without a statistical difference (Table 5). The average duration of late follow-up was 390.1 ± 289.1 days, with no difference between the groups. There was no difference between the groups regarding the variables associated with the need for new urgent revascularization, new infarction, or death (Table 6).

Data are presented as mean ± standard deviation or number (percentage).

*Number of lesions evaluated.

†In the ostial lesions, pressure equalization was performed with the catheter outside the coronary artery and the guidewire at the root of the aorta.

‡Type of physiological assessment that the vessels underwent.

§Functionally significant lesions with an iFR < 0.86 or FFR < 0.80. iFR values between 0.86 and 0.93 indicated conversion of the procedure to FFR.

Table 5: Procedural characteristics related to variables by number of lesions

Variable	A Group (N = 93)*	B Group (N = 37)*	General sample (N = 130)*	p value
Lesion territory – n (%)				
Left main	4 (4.3)	2 (5.2)	6 (4.6)	0.796
Left anterior descending artery	56 (60.2)	22 (59.4)	78 (60)	
Right coronary artery	14 (15)	5 (13.5)	19 (14.6)	
Left circumflex artery	18 (19.3)	6 (16.2)	24 (18.4)	
Arterial graft	0 (0)	1 (2.6)	1 (0.7)	0.116
Saphenous vein graft	1 (1)	2 (5.2)	3	
Lesion location – n (%)				
Ostial†	11 (11.8)	0 (0)	11 (8.4)	0.03
Proximal	31 (33.3)	13 (34.2)	44 (33.8)	0.890
Mid	40 (43)	18 (48.6)	58 (44.6)	0.720
Distal	10 (15.3)	4 (10.5)	14 (10.7)	0.993
Saphenous vein graft	1 (1)	2 (5.2)	3	
Diameter stenosis (%)	57.9 ± 12.1	69.4 ± 11.1	61.3 ± 12.9	<0.001
ISR	8 (8.6)	4 (10.5)	12 (9.2)	0.721
AHA classification – n (%)				
A	6 (6.4)	2 (5.2)	8 (6.1)	0.832
B1	30 (32.2)	8 (21)	38 (29.2)	0.364
B2	22 (23.6)	8 (21)	30 (23)	0.843
C	35 (53.8)	19 (51.3)	54 (41.5)	0.366
SCAI classification – n (%)				
I	58 (62.3)	19 (51.3)	77 (59.2)	0.553
II	35 (37.6)	18 (48.6)	53 (40.7)	0.461
Moderate to severe calcified lesion – n (%)	15 (16.1)	8 (21)	23 (28.7)	0.539
Intracoronary adenosine – n (%)	26 (27.9)	9 (24.3)	34 (26.1)	0.747
iFR performed – n (%)‡	93 (100)	37 (100)	130 (100)	0.887
iFR mean – n (%)	0.96 ± 0.04	0.8 ± 0.09	0.90 ± 0.08	<0.001
FFR performed – n (%)‡	25 (26.8)	9 (24.3)	34 (26.1)	0.818
FFR mean – n (%)	0.87 ± 0.04	0.79 ± 0.035	0.85 ± 0.03	<0.001
Revascularization of functionally significant lesions – n (%)§				
PCI	0 (0)	32 (86.4)	32 (24.6)	-
CABG	0 (0)	5 (13.5)	5 (3.8)	-
Reclassified the initial therapeutic decision – n (%)	26 (27.9)	14 (37.8)	40 (30.7)	0.430
Complications – n (%)‖	0 (0)	1 (2.7)	1 (0.7)	0.116

Group A: deferred lesions; Group B: revascularized lesions.

‖We had a case of intra-procedural complication of coronary artery dissection in Group B that required treatment with PCI with stent implantation.

AHA, American Heart Associate; SCAI, Society for Cardiovascular Angiography and Interventions; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; iFR, instantaneous wave-free ratio; FFR, fractional flow reserve.

Data are presented as mean ± standard deviation or number (percentage).

*Number of patients

TLR, target lesion revascularization; TVR, target vessel revascularization; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Table 6: Late follow-up

Variable	Group A (N = 65)*	Group B (N = 25)*	p value
Patients followed – n (%)	24 (96)	61 (93.8)	
Lost to follow-up – n (%)	1 (4)	4 (6.1)	0.977
Average segment time – n (%)	323.1 ± 305.8	416.5 ± 280.4	0.202
Repeat revascularization non-urgent – n (%)	2 (8)	3 (12)	0.689
PCI	2 (8)	0 (0)	0.08
CABG	0 (0)	1 (1.5)	>0.999
RIS – n (%)	1 (4)	0 (0)	>0.999
TLR non-urgent – n (%)	1 (4)	1 (1.5)	0.494
PCI	1 (4)	0 (0)	>0.999
CABG	0 (0)	1 (1.5)	>0.999
TVR non-urgent – n (%)	1 (4)	2 (3)	0.789
PCI	1 (4)	0 (0)	>0.999
CABG	0 (0)	2 (3)	>0.999
Nonfatal myocardial infarction – n (%)	0 (0)	0 (0)	-
Death from all causes – n (%)	0 (0)	2 (3)	>0.999
Cardiac death	0 (0)	0 (0)	-
Non cardiac death	0 (0)	2 (3)	> 0.999

Group A: deferred lesions; Group B: revascularized lesions.

TLR, target lesion revascularization; TVR, target vessel revascularization; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Discussion

Our findings indicate that the strategy for assessing coronary physiology with iFR is safe and effective in a real-world setting. In both groups, patients also had low rates of adverse cardiac events and death at late follow-up [6,7]. The results of our series align with other daily clinical practice records that assessed the benefits of coronary revascularization guided by invasive physiology. In the J-CONFIRM Registry [11], the target vessel failure rate was 5.5% in non-revascularized lesions, demonstrating the safety of the invasive physiology method when revascularization is rejected in daily clinical practice. In the IRIS-FFR study [12], the non-revascularization of coronary stenoses with FFR values >0.76 proved to be a

safe treatment strategy. Thus, our results suggest that the benefits of RCTs in iFR-guided coronary revascularization can also be achieved in the real world. The importance of observational data such as that obtained from clinical records is that they complement the scientific evidence of RCTs when demonstrating effectiveness in clinical practice.

Most patients in our series were classified into Group A, which shows that the isolated visual estimate is not a good parameter to guide the revascularization of intermediate lesions. In choosing to assess the physiology of the injury, we failed to perform many PCI procedures. However, the most important thing is that we did not fail to safely perform revascularization procedures since the patients' long-term outcomes were satisfactory. In other words, invasive physiology is a safe technique to indicate revascularization. Here, iFR was the physiology method used. The main advantage of iFR is the non-use of adenosine, which makes the procedure safer and more tolerable for the patient because the drug's side effects are avoided; furthermore, the procedure is faster and more economically viable when compared to FFR.

Some studies suggest the superiority of iFR in classifying coronary lesions when compared to FFR. In the JUSTIFY-CLEAR Study [13] iFR had a greater agreement with the coronary flow reserve than did FFR. However, in the same study, FFR was more likely to overestimate the severity of the lesion than iFR, probably because hyperemia causes a pressure decrease below the 0.80 threshold in lesions of intermediate severity despite normal coronary flow. Previous validation studies of the iFR method have also shown that the diagnostic accuracy of iFR is superior to that of FFR [14,15]. The iFR is more closely linked to the coronary flow reserve than the FFR, and the revascularization rates associated with the former were lower than the latter [16].

Our study's main limitations are that it is a single-center study, a registry, and not a randomized trial, and the number of patients is relatively modest. Future multi-center studies with a larger sample population are recommended.

In conclusion, our study showed the iFR-based invasive physiology method's safety as an indicator for coronary revascularization in daily clinical practice. Both groups of patients had low rates of adverse cardiac events and death in late follow-up.

References

1. Gibson CM, Safian RD. Limitations of cineangiography: impact of new technologies for image processing and quantification. Trends Cardiovasc Med. 1992; 2: 156-160.
2. Stadius ML, Alderman EL. Coronary artery revascularization. Critical need for, and consequences of, objetive angiographic assessment of lesion severity. Circulation. 1990; 82: 2231-2234.
3. Wong WH, Kirkeeide RL, Gould KL. Cardiac imaging and image processing. In: Collins SM, Korton S, ed. Computer applications in angiography. New York: McGraw-Hill. 1986.
4. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van' t Veer M, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009; 360: 213-224.
5. Batista SB, Raposo L, Santos L, Ramos R, Cale R, Jorge E, et al. Impact of routine fractional flow reserve evaluation during coronary angiography on management strategy and clinical outcome: one-year results of the POST-IT multicenter registry. Circ Cardiovasc Interv. 2016; 9: 1-10.
6. Götberg M, Christiansen EH, Gudmundsdottir IJ, Sandhall L, Danielewicz M, Jakobsen L, et al. Instantaneous wave-free ratio versus fractional flow reserve to guide PCI. N Engl J Med. 2017; 376: 1813-1823.
7. Davies JE, Sen S, Dehbi HM, Al-Lamee R, Petraco R, Nijjer SS, et al. Use of the instantaneous wave-free ratio or fractional flow reserve in PCI. N Engl J Med. 2017; 376: 1824-1834.
8. Petraco R, Park JJ, Sen S, Nijjer SS, Malik IS, Echavarría-Pinto M, et al. Hybrid iFR-FFR decision-making strategy: implications for enhancing universal adoption of physiology-guided coronaryrevascularization. EuroIntervention. 2013; 8: 1157-1165.
9. Rivero F, Cuesta J, Bastante T, Benedicto A, García-Guimaraes M, Fuentes-Ferrer M, et al. Diagnostic accuracy of a hybrid approach of instantaneous wave-free ratio and fractional flow reserve using high-dose intracoronary adenosine to characterize intermediate coronary lesions: Results of the PALS (Practical Assessment of Lesion Severity) prospective study. Catheter Cardiovasc Interv. 2017; 90: 1070-1076.
10. Escaned J, Echavarría-Pinto M, Garcia-Garcia HM, van de Hoef TP, de Vries T, Kaul P, et al. Prospective assessment of the diagnostic accuracy of instantaneous wave-free ratio to assess coronary stenosis relevance: results of ADVISE II international, multicenter study (ADenosine Vasodilator Independent Stenosis Evaluation II). JACC Cardiovasc Interv. 2015; 8: 824-833.
11. Kuramitsu S, Matsuo H, Shinozaki T, Horie K, Takashima H, Terai H, et al. Two-year outcomes after deferral of revascularization based on fractional flow reserve: The J-CONFIRM Registry. Circ Cardiovasc Interv. 2020; 13: e008355.
12. Ahn JM, Park DW, Shin ES, Koo BK, Nam CW, Doh JH, et al. Fractional flow reserve and cardiac events in coronary artery disease: data from a prospective IRIS-FFR registry (Interventional Cardiology Research Incooperation Society Fractional Flow Reserve). Circulation. 2017; 135: 2241-2251.
13. Sen S, Asrress KN, Nijjer S, Petraco R, Malik IS, Foale RA, et al. Diagnostic classification of the instantaneous wave-free ratio is equivalent to fractional flow reserve and is not improved with adenosine administration: results of CLARIFY (Classification Accuracy of Pressure-Only Ratios Against Indices Using Flow Study). J Am Coll Cardiol. 2013; 61: 1409-1420.

14. Sen S, Nijjer S, Petraco R, Malik IS, Francis DP, Davies J. Instantaneous wave-free ratio: numerically different, but diagnostically superior to FFR? Is lower always better? J Am Coll Cardiol. 2013; 62: 566.

15. van de Hoef TP, Meuwissen M, Escaned J, Sen S, Petraco R, van Lavieren MA, et al. Head-to-head comparison of basal stenosis resistance index, instantaneous wave-free ratio, and fractional flow reserve: diagnostic accuracy for stenosis-specific myocardial ischaemia. EuroIntervention. 2015; 11: 914-925.

16. van de Hoef TP, van Lavieren MA, Damman P, Delewi R, Piek MA, Chamuleau SAJ, et al. Physiological basis and long-term clinical outcome of discordance between fractional flow reserve and coronary flow velocity reserve in coronary stenoses of intermediate severity. Circ Cardiovasc Interv. 2014; 7: 301-311.