SHORT REPORT

Submitted: 23.10.2021; Accepted: 19.11.2021; Published online: 23.02.2022

Pre-angioplasty instantaneous wave-free ratio pullback predicts hemodynamic outcome in diffuse coronary artery disease

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Abstract

Background: Serial stenoses or diffuse vessel narrowing hamper pressure wire–guided management of coronary stenoses. Characterization of functional relevance of individual stenoses or narrowed segments constitutes an unmet need in ischemia-driven percutaneous revascularization.

Aim of the Study: To perform hemodynamic mapping of the entire vessel using pullback technique of a pressure guidewire with continuous instantaneous wave-free ratio (iFR) measurement compared coronary angiography aiming to minimize the procedure, decrease number and length of stents used.

Materials and Methods: This study was conducted on 40 patients presented with diffuse coronary artery disease and undergoing elective PCI. Diagnostic coronary angiography using the routine angiographic projections was done with assessment of non-obstructive coronary lesions by 2D quantitative coronary angiography and iFR pullback measurement

Results: Percentage of difference between probable sig lesions via pullback technique and No of actual sig lesions for studied group, was (59.5%). The difference was statistically highly significant p=0.0001.

Conclusion: Compared with angiography alone, availability of iFR pullback data significantly decreased the number and length of hemodynamically significant lesions identified for revascularization.

Keywords

Coronary artery disease, Instantaneous wave-free ratio, Physiological lesion assessment, Stenosis

Imprint

Ahmed Youssef Nammour, Hisham Mohamed Aboul-Enein, Mohammed Hamouda, Ahmed Atef Elhelaly. Pre-angioplasty instantaneous wave-free ratio pullback predicts hemodynamic outcome in diffuse coronary artery disease. Cardiometry; Issue 21;February 2022; p. 95-101; DOI: 10.18137/cardiometry.2022.21.95101; Available from: http://www.cardiometry.net/issues/no21-february-2022/pre-angioplasty-instantaneous-wave-free

Introduction

The presence of myocardial ischemia is a significant risk factor for an adverse clinical outcome. Revascularization of obstructive coronary lesions that induce ischemia can improve a patient's functional status and outcome [1].

For stenotic lesions that do not induce ischemia, however, the benefit of revascularization is less clear, and medical therapy alone is likely to be effective [2].

With the introduction of drug-eluting stents (DES), the percentage of patients with multivessel coronary artery disease in whom percutaneous coronary intervention (PCI) is performed has progressively increased [3]. However, in patients with multivessel coronary artery disease (MVD), determining which lesions cause ischemia and deserve stenting can be challenging. Noninvasive stress imaging studies has limited ability to accurately confine ischemia-producing lesions in these patients [4]. Although coronary angiography may underestimates /overestimates a lesion's functional severity, it is still the standard technique to guide PCI in patients with MVD [5].

Pressure wire technology has revolutionized the treatment of coronary disease, by identifying clinically important stenoses. Physiology provides an objective marker to support intervention by identifying hemodynamically significant lesions However, most used physiological indices have limited ability to isolate individual lesion significance in vessels with multiple lesions. The prevalence of such diffuse coronary disease is increasing and accurate assessment to guide appropriate therapy is paramount [6, 7].

Instantaneous wave-free ratio (iFR) is a resting index of stenosis severity that is measured without a vasodilator. It is the ratio of distal and proximal pressures over the wave-free period, a specific part of diastole during which coronary flow velocity is naturally at its highest (8). This higher flow velocity allows iFR to assess higher pressure gradients across stenoses than possible by using the complete cardiac cycle whilst also preserving the key characteristic of constant flow [9]. For the iFR-only strategy, the used a cut-off value of 0.89 below which it is considered a significant stenosis [10].

As a result, iFR has a greater ability to identify small gradients pertinent to the assessment of a diffusely diseased vessel [9,11].

The value of mapping the iFR intensity in diffusely diseased vessels enables identification of any focal areas of disease that may cause the predominant pressure loss, and therefore be targeted for percutaneous intervention. The percentage contribution of pressure loss can be displayed to assist decision-making. The mapping can be displayed in a number of different ways. With co-registration, the pressure wire pullback can become integrated with the angiographic findings to enhance the ease of understanding of the data. 'Dots' representing units of pressure loss can help identify which stenoses are most hemodynamically important. In addition, iFR intensity plotted as a function of distance can give additional information regarding the length over which the pressure drop occurs. This may assist in identifying which lesions in the vessel contribute most to pressure loss and allow operators to estimate the physiological length of a stenosis to help decide between different revascularization strategies [12].

Quantitative coronary angiography (QCA) can be used as another method to help assessment of the coronary lesions. Although intravascular ultrasound (IVUS) currently yields the most accurate measurements of vessel geometry and lesion severity [13]. QCA measurements can be performed on existing standard coronary angiography images without the need for additional time or equipment during the procedure [14].

Resistance to coronary blood flow can be divided into three major components: epicardial arteries, arterioles and microcirculatory resistance arteries and extravascular resistance. There is no measurable pressure drop in the epicardial arteries although in the presence of hemodynamically significant epicardial artery narrowing (more than 50% diameter reduction), the resistance at this level contributes as an important component to the total coronary resistance [15].

Aim of the work

To perform hemodynamic mapping of the entire vessel using pullback technique of a pressure guidewire with continuous instantaneous wave-free ratio (iFR) measurement compared coronary angiography aiming to minimize the procedure, decrease number and length of stents used.

Patient and methods

This non randomized controlled trial was conducted at Cardiology Department, Benha University and NHI during the period from August 2020 to August 2021. The study included a group of 40 patients presented with diffuse coronary artery disease and undergoing elective PCI.

Inclusion Criteria

Patients undergoing elective PCI with diffuse coronary artery disease.

Exclusion criteria

The individuals with the following criteria were excluded from our study; acute MI, simple obstructive and non-obstructive coronary artery lesions, LM lesions, small vessel disease less than 2 mm diameters and myocardial bridge.

Withdrawal criteria

The patient has the right to withdraw from the study at any time without any negative consequence on the treatment plane.

All patients were subjected to the following

Complete history taking including age, gender and presence of risk factors for CAD, physical examination, twelve leads ECG, laboratory investigations and echocardiography.

Coronary angiography and PCI

Coronary angiography was performed using conventional approaches. Patients underwent a diagnostic coronary angiogram according to the routine clinical practice of the participating center. Angiographic inclusion criteria included the presence of a ≥ 40% stenosis by visual estimate in any major epicardial vessels or any major branch. After angiography, the angiographic images were reviewed, and operators were asked to prospectively document their plans for angioplasty on an electronic case report form. Specifically, operators were required to record the number of angiographically significant lesions and the total lesion length(s) requiring stenting for each patient. This planning phase, based on visual assessment of angiographic data, was completed before any physiological measurements with iFR pullback.

iFR pullback measurement

Intracoronary nitrates (300 mg) were administered in all cases before pressure wires were introduced. Pressure wire (Prestige guide wire PLUS/Verrata guide wire; Philips/Volcano, Amsterdam, the Netherlands) normalization was performed at the coronary ostia before each recording and before resting pressure wire pullback was performed. iFR was measured in the distal position of the target vessel, followed by an iFR pullback recording along the length of the vessel under resting conditions. Pressure wire pullback was performed in a manual (96.4%) or mechanized manner (3.6%) using Volcano pullback device R100. Pullback speed was w0.5 to 1.0 mm/s and was continued until the pressure sensor reached the left main stem ostium or right coronary ostium. During the pressure wire pullback, regular fluoroscopic recordings of the wire position were performed with accompanying bookmarks on the iFR pullback trace. This allowed operators to determine the trans-stenotic pressure gradient (in iFR units) for each lesion of interest along the entire length of the diseased vessel. In this study, automatic coregistration of the iFR pullback curve with the angiogram was not yet available and thus was not performed.

Post-PCI iFR prediction

According to the aforementioned technique, iFR pullback was used to quantify the iFR gradient at each lesion location of interest along the length of the vessel. The predicted post-PCI iFR (iFRpred) was calculated by summation of the iFR gradient(s) with the distal vessel iFR value. In line with the threshold value used in recent iFR clinical outcome trials (3,4), a post-PCI iFR value ≤ 0.89 was considered suboptimal. Accordingly, operators tailored their PCI approach to achieve a post-PCI iFR value >0.89. At this stage, operators were once more asked to record their interventional strategy with respect to the number and length of lesions to stent based on the addition of iFR pullback to angiogram data.

Post-PCI iFR measurement

Angioplasty was performed as per usual clinical practice using third generation drug-eluting stents, which were all angiographically optimized. Following successful PCI, measurement of the observed post-angioplasty iFR (iFRobs) was performed with the pressure sensor positioned at an identical coronary location as before.

Statistical analysis

All data were collected, tabulated and statistically analyzed using (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.2015). Quantitative data were expressed as the mean ± SD & median (range), and qualitative data were expressed as & (percentage). Wilcoxon Signed Ranks Test was used to compare between two paired of not normally distributed variable. McNemar test was used to compare between two paired of categorical variable. All tests were two sided.

Results

Table 1
Demographic data for studied group

variables	Studied group (n=40)
Age per year Mean ±SD range	56.87±8.63 38 -74
sex Males Females	 24(60%) 16(40%)
HTN	24 (60%)
DM	26 (65%)
Dyslipidemia	25 (62.5%)
Smoking	22 (55%)

This table shows the mean age of all studied patients was 56.87±8.63 years with range (38-74), 24 of them males (60%), HTN represented 60%, DM 65.0%, dyslipidemia, 62.5% and smokers represented 55%.

Table 2
Difference between No of probable sig lesions via 2D assessment and No of actual sig lesions by IFR among studied group (n.40)

	No of probable sig lesions by 2D assessment	No of actual sig lesions After IFR	Percentage of difference	w	P
Mean ±SD Median Range	3.7±0.93 4 (2-6)	1.5±0.64 1 (1-3)	(59.5%)	5.58	0.0001 (HS)

W = Wilcoxon Signed Ranks Test (HS) p<0.001 highly significant

The above table shows median of lesion via 2D assessment was 4 with range (2-6) higher than detected actually. Percentage of difference between probable sig lesions via 2D assessment and No of actual sig lesions by IFR for studied group, was (59.5%). The difference statistically highly significant p=0.0001.

Table 3
Difference between length expected to be covered mm via 2D assessment and area actually covered after IFR assessment mm among studied group (n. 40)

	Length expected to be covered (mm)	Length covered after IFR (mm)	Percentage of difference	w	P
Mean ±SD Median Range	61.3± 12.56 59 (38-92)	36.3± 19.25 37 (0-72)	(40.8%)	5.37	0.0001 (HS)

W= Wilcoxon Signed Ranks Test (HS) p<0.001 highly significant

The above table shows median length expected to be covered (mm) via 2D assessment was 59 with range (38–92) higher than detected actually by IFR. Percentage of difference between length expected to be covered (mm) via 2D assessment and area covered (mm) after IFR study for studied group, was (40.8 %).The difference statistically highly significant p=0.0001.

Table 4
Comparison between need of stents expected via 2D assessment and stent deployed after IFR study for studied group (n.40)

	Expected stent needed n. (%)	stent deployed n. (%)	MC p
Stent needed	40(100.0)	34(85)	0.031 (S)
No Stent needed	0(0.0)	6(15)	

MC-Nemar test (S) p<0.05 significant

This table shows all patients Stent needed via pullback technique. while only 34(85%) actually need stent application the difference statistically significant p<0.05.

Table 5
Comparison between number need of stents expected and number stent deployed after pullback technique for studied group (n.40)

	number need of stents expected n. (%)	Number stent deployed n. (%)	MCp
one stent			
yes	1 (2.5%)	23(57.5%)	0.0001 (HS)
No	39(97.5%)	17(42.5%)	
Two stents			
yes	25 (62.5%)	11(27.5%)	0.015 (S)
No	15(37.5%)	29(72.5%)	
Three stents			
yes	14 (35%)	0(0.0%)	0.0001 (HS)
No	26(65%)	40(100%)	

MC-Nemar test (S) p<0.05 significant (HS) p<0.001 highly significant

This table show s one Stent needed via pullback technique is lower than stent deplored p=0.0001. Moreover 25(62.5%) of patients need two stent via pullback technique versus 11(27.5%) of patients need actually two stent application the difference statistically significant p=0.015. finally 14(35%) of patients need three stent via pullback technique but non of patients need actually three stents application the difference statistically highly significant p=0.0001.It obvious there is discrepancy between Stent needed via pullback technique and actual number of stents needed.

Table 6
Multiple linear regression model for predict area covered mm among studied patients (n.40):

	Unstandardized Coefficients					
	β	Std. Error	t	Sig.	r	R2
(Constant)	-68.019	23.574				
length expected to be covered mm	0.844	0.206	4.101	0.0001	0.607	0.369
age per years	0.924	0.299	3.086	0.004		

Regression coefficients(β): represent the mean change in the dependent variable (area covered mm) for one unit of change in the predictor variables. (Std. Error): are the standard errors of the regression coefficients
R square = 36.9 % of predictors Model ANOVA: F=10.8, p=0.0001

Significant predictors of area covered mm were length expected to be covered mm by (Wave-Free Ratio Pullback) and patient's age per years.

Significant predictor of number of affected area was No of probable sig lesions by (Wave-Free Ratio Pullback).

Table 7
Simple linear regression model for prediction of number of affected area among studied patients (n.40):

	Unstandard-ized Coeffi-cients		t	Sig.	r	R2
	β	Std. Error				
(Constant)	0.015					
No of proba-ble sig lesions	0.405	0.090	4.52	0.0001	0.591	0.35

Regression coefficients(β): represent the mean change in the dependent variable (area covered mm) for one unit of change in the predictor variables. (Std. Error): are the standard errors of the regression coefficients
R square = 35 % of predictor Model ANOVA: F=20.426, p=0.0001

Discussion

In our study we aimed to perform hemodynamic mapping of the entire vessel using pullback technique of a pressure guidewire with continuous instantaneous wave-free ratio (iFR) measurement compared coronary angiography aiming to minimize the procedure, decrease number and length of stents used.

In the current study, the median of lesion via 2D assessment was 4 with range (2-6) higher than detected actually. Percentage of difference between probable sig lesions via 2D assessment and No of actual sig lesions by IFR for studied group, was (59.5%). The difference statistically highly significant p=0.000. In agreement with our study, Kikuta et al. [16] found that the number of coronary lesions determined as hemodynamically significant according to angiographic appearance versus iFR pullback. In 47 of 159 patients (30%) and in 52 of 168 vessels (31%), the number of lesions to treat was changed after iFR pullback measurement. On a per-patient basis, the addition of iFR pullback data decreased the number of lesions identified for revascularization from 1.42±0.05 following angiographic assessment alone to 1.23±0.05 (p = 0.0001 for difference).

In the present study, median length expected to be covered via 2D assessment was 59 with range (38-92) higher than detected actually by IFR. Percentage of difference between length expected to be covered via 2D assessment and area covered (mm) after IFR study for studied group, was (40.8 %).The difference statistically highly significant p=0.0001. In agreement with our study, Kikuta et al. [16] found that the availability of iFR pullback data decreased the total lesion length identified for revascularization from 31.3±1.3 mm after angiography alone to 26.9±1.3 mm after iFR pullback (p < 0.0001 for difference). Disagreement between total lesion length identified by angiography alone and iFR pullback occurred in 118 patients (74%) in 121 vessels (72%).

Also, all patients needed stent via pullback technique while only 85% actually need stent application via 2D assessment, leading to a fewer stents placed per patient. The difference was statistically significant p<0.05. This came in agreement with Younus, et al., [17], who found that there were significantly fewer hemodynamically significant lesions as assessed by iFR, leading to a fewer stents placed per patient.

The ease of iFR measurement facilitates and encourages the measurement of multiple vessels. And also, iFR-GRADIENT showed there was a significant decrease in the number and length of hemodynamically significant lesions planned for revascularization [18]. Also, Kikuta et al. [16] demonstrates in their multicenter registry study that online iFR pullback performed under resting conditions predicted the physiological outcome of PCI with a high degree of accuracy. They found that Compared with angiography alone, availability of iFR pullback data significantly decreased the number and length of hemodynamically significant lesions identified for revascularization. Overall, revascularization procedural planning was altered in nearly one-third of patients.

Park et al. [19] found that before physical PCI is commenced, iFR pullback data can inform the clinician whether their proposed strategy will improve coronary physiology sufficiently to achieve a physiologically favorable outcome.

The iFR grounds on the concept that at a specific time in diastole – the so-called wave-free period – intracoronary pressure and flow decline together in a linear fashion, whereas microvascular resistance remains more stable and significantly lower than the rest of cardiac cycle. Therefore, over this period, the pressure gradient across coronary stenosis can be measured obviating generating hyperemia through adenosine infusion. Another advantage of iFR is the ability to individually assess lesions severity in the context of diffuse vessel disease. Specifically, by using the coregistration of the iFR pullback trace and the coronary angiogram (ie, plotting measured values directly over angiographic views), iFR is able to detect lesion-specific pressure drop along the whole length of the vessel and differentiate focal from diffuse coronary disease. This allows the cardiologist to (1) properly identify which lesion/s should be treated (if any), (2) accurately predict to what extent coronary physiology will improve after PCI per each lesion, and (3) confidently decide the number, length, and position of stents to be used to pursue a successful procedure (20).

iFR showed excellent diagnostic test characteristics when compared with other invasive and non-invasive measures of stenosis severity and myocardial ischaemia [21].

In the present study, significant predictors of area covered mm were length expected to be covered mm by (Wave-Free Ratio Pullback) and patient's age per years. Kikuta et al. [16] found that the only univariate and multivariate predictor identified for the difference between both groups was iFR pullback measurement in culprit vessels in patients with acute coronary syndrome (ACS). Age, sex, diabetes mellitus, hypertension, hyperlipidemia, creatinine, smoker, pre-PCI iFR, and number of lesions were not significant predictors of the difference between both groups. Jeremias, [22] found that the available clinical evidence strongly supports the current practice of an ischemia-guided revascularization strategy, in which lesions with abnormal invasive physiology benefit from revascularization, whereas lesions with negative physiology can be safely deferred. It seems that this basic principle holds true regardless of whether FFR or iFR is used for clinical decision-making.

Furthermore, iFR showed excellent diagnostic test characteristics when compared with other invasive and non-invasive measures of stenosis severity and myocardial ischaemia such as the hyperaemic stenosis resistance index, coronary flow reserve (CFR), and positron emission tomography [21].

Conclusion

This study demonstrates that iFR pullback performed under resting conditions predicted the physiological outcome of PCI with a high degree of accuracy. Compared with angiography alone, availability of iFR pullback data significantly decreased the number and length of hemodynamically significant lesions identified for revascularization.

Limitations:

- The selection bias cannot be excluded because the patient enrollment was not totally consecutive and the selection of target vessels was left to the discretion of operators. However, patients were prospectively recruited for a short period of time to minimize the bias.
- Although we assessed iFR gradients on the basis of coronary segments, it also might have been possible to assess them based on coronary lesions. However, since our target vessels consist of not only tandem but also focal and diffuse lesions, the segmental assessment was the only way to assess the reproducibility in our population.
- Potential sources of operator error include differences in the mental coregistration of the angiographic position of the pressure gradient on the iFR pullback curve. In this study, operators were required to observe physiological pullback data and angiographic information at the same time and mentally coregister the 2 pieces of information.
- Furthermore, visual angiographic grading of lesion length is likely to have varied between operators, but this practice remains representative of routine clinical care.

Financial support and sponsorship

Nil

Statement on ethical issues

Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest

None declared.

Author contributions

The authors read the ICMJE criteria for authorship and approved the final manuscript.

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