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Evaluating the Impact of Fractional Flow Reserve (FFR) on Decision-Making for Treatment of Borderline Coronary Artery Lesions: MUST University Experience, Egypt

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ABSTRACT

Background: The primary reference criterion for evaluating coronary artery stenosis functional significance is fractional flow reserve (FFR). It helps the interventionist to define appropriate angiographic borderline coronary lesions that should or should not be treated with a stent.

Objective: To evaluate the experience of the cardiology department, MUST University, on the use of FFR and its impact on patients with a borderline coronary lesion as regard revascularization decision-making.

Patients and methods: A retrospective study were done on 86 patients with borderline lesions undergoing coronary angiograms for whom FFR was performed. Three experienced cardiac interventionists re-analyzed their coronary angiography and whether to delay or conduct revascularization with borderline stenotic lesions (40-70 %). A distinction was made between the findings of quantitative coronary angiography (QCA), visual and functional assessment of coronary stenosis severity. **Result:** Eighty-six patients (51 males and 35 females) with a mean age of 58.60 ± 9.20 were enrolled in the current study. FFR was < 0.80 in 26.74% (23/86) of the patients, and they had coronary angioplasty. Between quantitative evaluation of lesion diameter by FFR and visual measurement, the correlation was -0.645 ***(P*** < 0.001). Seven patients (8.139%) had FFR > 0.8 left main (LM) lesion and for the other vessels with severe coronary lesions, stenting was performed.

Conclusion: In patients having borderline coronary artery stenosis, FFR is an important tool for clinical decisions making about procedures of revascularization. FFR results in alteration in the coronary intervention judgment.

Keywords: Coronary Angiography, Coronary Stenosis, Fractional Flow Reserve.

INTRODUCTION

The definition of a borderline coronary artery lesion is a diameter that narrows from about 40 to about 70 %. It can be identified in approximately one-third to half of the coronary angiograms. Visual assessment of the severity of coronary lesions during routine coronary angiography is not always reliable due to the two-dimensional views and inter/intra-observer variability [(1, 2)]. The hemodynamic influence of coronary artery stenosis can be determined by fractional flow reserve (FFR) measurements. In the absence of non-invasive evidence of ischemia, current guidance suggests their use. The prognostic effect of FFR has been tested, and it has been shown that revascularization can be safely postponed if FFR is > 0.80, whereas stenosis revascularization with FFR values of 0.80 results in substantially lower rates of events compared to medical therapy. In patients with borderline severity of coronary artery stenosis and angina pectoris, decision-making for choosing treatment options, revascularization, or medical follow-up is a challenge, as determined by visual estimation for a coronary angiogram. Coronary artery revascularization is done in a significant number of patients with no definite evidence that symptoms are caused by coronary stenosis [(3-7)].

Technical developments in recent years have equipped catheterization laboratories with innovative testing instruments to assess the coronary artery lesions severity. Myocardial FFR is defined as an invasive index of the coronary stenosis functional severity in borderline lesions, according to pressure flow study of the coronary lesion in the maximum flow reserve [(8-9)].

Fractional flow reserve (FFR) is one of the best diagnostic methods used for determining the functional value of borderline coronary lesion. This can be achieved through intracoronary pressure guide wires. FFR can also be calculated as the ratio of the maximum coronary blood flow in the stenotic area to the maximum blood flow in the normal part of the same artery. FFR = Pd (the distal coronary artery mean pressure) /Pa (aortic pressure) during maximal hyperemia. The index of FFR is independent of heart rate, systemic blood pressure, and systolic function of the left ventricle. It is also not affected by situations known to improve baseline myocardial blood flow. Regardless of the patient or particular vessel examined, the normal index value is one. It has been shown that the FFR corresponds well with other non-invasive ischemia detection tests. FFR has clear clinical importance, unlike most other invasive indices [(3, 4, 8, 10-12).] FFR was first used as part of a clinical trial in Egypt in 2013 and was used in clinical practice in 2015. It was first used in our catheter lab at Misr University for Science and Technology (MUST) hospital in 2016.

Borderline coronary artery lesions may be stented incorrectly without using FFR. Using FFR improves

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patient outcomes, reduces the number of stents inserted by around 25%, and is more cost-efficient for patients [1,13,14].

AIM OF STUDY

This research aimed at evaluating the experience of the Cardiology Department at MUST University about the influence of FFR on the revascularization decision-making technique in borderline coronary artery lesion patients.

PATIENTS AND METHODS

A retrospective study enrolled 86 patients with borderline stenotic lesions, 40-70% by coronary angiography, for whom FFR was performed at the period from in the period between December 2016 and November 2019.

Ethical approval:

The study was approved by the MUST university Ethical Committee board.

We analyzed all demographic and clinical data. Three qualified interventional cardiologists (blinded to FFR results) re-analyzed all patients with respect to coronary angiography to assess their angiographic lesion severity and whether revascularization should be delayed or performed.

Through the visual estimation of two cardiologists independently, diameter stenosis of 40%–70% was defined as a borderline coronary artery lesion. If they had different estimations, the opinion of the third cardiologist was deemed to be the final decision.

The target vessel was a lesion with more than 2.5 mm reference vessel diameter in either the proximal or mid part of the main coronary artery. If the FFR was < 80%, percutaneous coronary intervention (PCI) was done.

Intracoronary administration of 200 μg nitroglycerin. A zero-calibrated 0.014" pressure guidewire was introduced in the coronary artery and placed distal to the evaluated stenosis. During maximal hyperemia and by using the Pd/Pa ratio, FFR was estimated. Pd is the mean coronary pressure distal to the stenosis section as determined by the pressure wire, whereas Pa denotes the mean aortic pressure as determined by the guiding catheter. Intracoronary adenosine (about 30 μg in the right and 40 μg in the left coronary arteries) produced the greatest hyperemia (7). Patients who needed FFR were identified on the basis of coronary lesions severity visual assessment by at least two cardiologists in each coronary artery.

Blinded to clinical and FFR data, a single operator carried out a quantitative coronary angiography on borderline coronary lesions offline. For quantitative coronary measurements, the most severe narrowing in a non-foreshortening view was chosen (Siemens Healthcare GmbH, Siemens software, Germany); the length of the lesion was estimated and documented.

Statistical analysis

SPSS software version 20 was used to analyze the data (Chicago, IL, USA). For continuous variables, data were expressed as mean ±standard deviation. For categorical variables, counts and percentages were used. The Kolmogorov-Smirnov test was employed to determine data distribution. The t-test was used for comparing the mean vascular and the minimal luminal diameters in individuals with FFR ≥ 0.80 vs those with lower values. Correlation between numerical variables was assessed by Pearson's correlation. Least square method was used for linear regression analysis. All tests were two-sided. Statistical significance was defined as $P < 0.05$.

RESULTS

The current retrospective study included 86 patients whose FFR was done in the period from December 2016 until November 2019. Our catheter laboratory performed 2520 angiography and interventional procedures.

As shown in table 1; the study included 86 participants (51 males and 35 females) with a mean age of 58.60 ± 9.20 years (range 45-70) who satisfied the inclusion criteria and were receiving clinically recommended coronary angiography. Table 1 summarizes the patients' clinical characteristics and standard risk factors of atherosclerosis.

Table (1): Baseline demographic and clinical characteristics of the patients:

Variable	Total (n=86)
Female	35 patients (40.70%)
Male	51patients (59.30%)
Age	58.60 ± 9.20 years
Family history	28 patients (32.56%)
Diabetes mellitus	31 patients (36.05%)
Smoking	41 patients (47.67%)
Hypertension	47 patients (54.65%)
Dyslipidemia	42 patients (48.84%)
Left ventricular ejection fraction	52.76 ± 4.58%

Table (2) shows angiographic results of all the studied population. Visual estimation of coronary artery diameter stenosis was 59.6 ±8.00%. Quantitative coronary angiography (QCA) was as follows ;(1) reference diameter was 3.25 ± 0.49 mm, (2) coronary artery diameter stenosis was 56.60 ± 7.80%, (3) Lesion length was14.00 ± 4.60 mm. FFR measures were 0.85±0.08. Vessels affected were as follow; (1) right coronary artery 33 patients (38.37%), (2) left main 7 patients (8.139%), (3) left anterior descending 57 patients (66.27%) and left circumflex17 patients (19.76%). Number of diseased vessels were as follow; (1) one vessel disease was 60 patients (69.67%), two vessels disease was 24 patients (27.90%) and three vessels disease was 2 patients (2.32%).

Table (2): Angiographic results of the study population:

Variable	
Visual estimation	
Diameter stenosis	59.60 ± 8.00%
QCA (Quantitative coronary angiography)	
Reference diameter	3.25 ± 0.49 mm
Diameter stenosis	56.60 ± 7.80%
Lesion length	14.00 ± 4.60 mm
Fractional flow reserve	0.85 ± 0.08
Vessels affected **Right coronary artery** **Left main** **Left anterior descending** **Left circumflex**	 33 patients (38.37%) 7 patients (8.139%) 57 patients (66.27%) 17 patients (19.76%)
Number of diseased vessels **one vessel disease** **two vessels disease** **Three vessels disease**	 60 patients (69.67%) 24 patients (27.90%) 2 patients (2.32%)

As shown in figure 1, the correlation coefficient between FFR and lesion diameter visual estimation was -0.645 (P< 0.001). FFR and coronary lumen stenosis showed a correlation of -0.482 (P = 0.008). FFR and lesion length showed a correlation of -0.671 (P<0.001). Visual estimation and quantitative measurement of lesion diameter showed a correlation of 0.851 (P < 0.001).

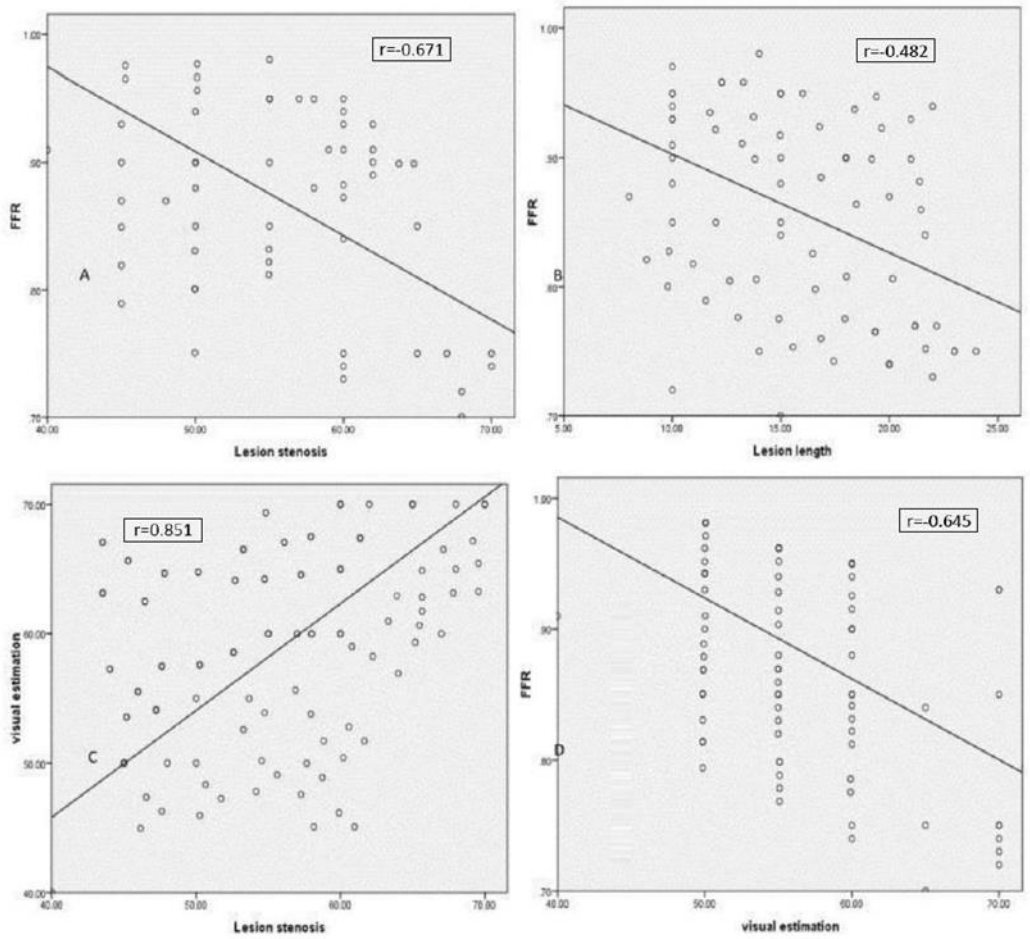

Figure (1): Fractional flow reserve correlation and regression curves versus visual and quantitative coronary lesions indices

Table (3): Treatment strategy of the study population:

Treatment strategy	Total (n=86)
PCI on target vessel (FFR<0.80)	23 (26.74)
Medical (FFR>0.80)	58 (67.45)
PCI on non-target vessel (FFR of target vessel is > 0.80)	5 (5.81)

PCI: Percutaneous coronary intervention.

As shown in table 3, FFR was less than 0.8 in 26.744% (23/86) of patients who, using a drug-eluting stent, had coronary angioplasty and stenting. Five patients (5.813%) had an FFR of more than 0.80 in the borderline lesion, while the other arteries with extensive lesions and stenosis more than 70% were stented. The FFR of the remaining patients was greater than 80%, and no revascularization was done.

Angiographic assessment alone leads to nearly 24% wrong classification of coronary lesions in the current study, and this was overcome by using FFR.

Left main (LM) coronary artery patients (8.139%) with intermediate lesions were included in this study (Table1). If FFR tests revealed no evidence of significant LM disease, the approach for revascularization would shift away from urgent coronary bypass graft surgery toward other arteries serious lesions stenting. Eight patients had transient severe bradycardia, and one patient experienced transient complete heart block following coronary adenosine injection.

DISCUSSION

This study provided our experience in the evaluation of borderline coronary stenosis by using coronary stenosis fractional flow reserve (FFR) in the cardiology department, Faculty of Medicine MUST University.

Routine coronary angiography, in contrast to FFR, is ineffective in determining the functional significance in borderline lesions with a 50-70% stenotic range. This is due to inter-/intra-observer variability, which is around 26% and 14%, respectively [(2)]. Because of more radiation exposure, price, a higher probability of using more contrast volume, and time limit, some of our center physicians did not use measurements of FFR in the assessment of the coronary stenosis severity.

The current study revealed that procedures of FFR measurement are prudent, leading to a reduction in exposure to radiation and no change in the amount of compared to conditions with improper PCI, and this was in accordance with **Leesar *et al.* [(15)].**

The technological advances in coronary catheters have made new and better-designed tools available. The complexity of the instruments, their costs, their restricted scope of use, or the scant yield of relevant knowledge means that modern devices are only used for research issues in a few hemodynamic laboratories or in occasional [(16)].

Although myocardial single-photon emission tomography (SPECT) showed a 90% or more sensitivity in multivessel coronary artery disease detection, the precision of the identification of each individual stenosis is limited. The relationship between target vessels and perfusion deficits is a frequent problem in these patients because detecting reversible perfusion abnormalities, especially of the culprit lesion, might fail [(17)]. Multivessel coronary artery disease was involved in some of the cases in the present study, so myocardial perfusion SPECT may be insignificant in the functional assessment of borderline lesions. FFR was of great importance in the clinical decision for either revascularization or medical treatment. **Leesar *et al.*** [(15)] found that, compared with stress perfusion scintigraphy, the FFR greatly shortens the length of hospitalization.

In the current study, physicians in our center use the FFR in less than 0.5% of the interventional procedures, but it had a strong negative impact on the need for revascularization in the borderline lesion. Numerous researches showed that FFR values greater than 0.75-0.80 were reliable predictors of favorable clinical outcomes in patients with intermediate LM disease. [(6, 18, 19)].

In the present study, FFR measurement of borderline lesion of left main (LM), proximal left anterior descending (LAD), or left circumflex (LCX) could change the revascularization strategy, coronary artery bypass grafting (CABG), stenting, or medical treatment if FFR showed insignificant lesions in LM.

This present research revealed that the lesion length and stenosis severity predicted lower FFR. FFR calculation is therefore sufficient to classify intermediate LM stenosis patients in whom excellent results can be associated with revascularization postpone, and this is in accordance with **Elfaramawy *et al.* [(12)].**

In this study, FFR demonstrated significant stenosis in just 23 (26.744%) lesions out of 86 patients with coronary stenting, so this procedure stopped other patients from being improperly stented (73.256%). In 58 patients (67.44%), the clinical decisions were shifted from PCI or CABG to medical treatment. The current small sample size research showed that FFR could not only alter patients' care strategy but also improve clinical and economic outcomes by minimizing unnecessary PCI [(2, 6)].

LIMITATIONS

This research included a relatively small number of patients.

CONCLUSION

In patients with borderline coronary artery lesions, FFR is a valuable method in clinical decisions making regarding procedures of revascularization. FFR results in alteration of the coronary intervention judgment, especially in patients with LM and multivessel disease.

RECOMMENDATION

Our study recommends the use of functional assessments by FFR for borderline coronary artery lesions in our and other catheterization laboratories.

REFERENCES

1. **Achenbach S, Rudolph T, Rieber T *et al.* (2017):** Performing and interpreting fractional flow reserve measurements in clinical practice. Interv Cardiol., 12(2):97-109.
2. **Tonino P, Fearon W, De Bruyne B *et al.* (2010):** Angiographic versus functional severity of coronary artery stenosis in the FAME study fractional flow reserve versus angiography in multivessel evaluation. J Am Coll Cardiol., 55 (25):2816-21.
3. **Iguchi T, Hasegawa T, Nishimura S *et al.* (2013):** Impact of lesion length on functional significance in intermediate coronary lesions. Clin Cardiol., 36 (3):172–7.
4. **Tonino P, De Bruyne B, Pijls N *et al.* (2009):** Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med., 360 (3):213–24.
5. **Moses J, Leon M, Popma J *et al.* (2003):** Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med., 349 (14):1315–23.
6. **Khosravi A, Pourbehi M, Pourmoghaddas M *et al.* (2015):** Evaluating the impact of fractional flow reserve-guided percutaneous coronary intervention in intermediate coronary artery lesions on the mode of treatment and their outcomes: An Iranian experience. ARYA Atherosclerosis, 11(2): 153–159.
7. **Kern M, Puri S, Craig W *et al.* (1998):** Hemodynamic rounds series II: Coronary hemodynamics for angioplasty and stenting after myocardial infarction: use of absolute, relative coronary velocity and fractional flow reserve. Cathet Cardiovasc Diagn., 45(2):174–82.
8. **Pijls N, van Son J, Kirkeeide R *et al.* (1993):** Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. Circulation, 87(4):1354–67.
9. **Pijls N, Van Gelder B, Van der Voort P *et al.* (1995):** Fractional flow reserve. A useful index to evaluate the influence of an epicardial coronary stenosis on myocardial blood flow. Circulation, 92 (11):3183–93.
10. **Pijls N, Bech G, El Gamal M *et al.* (1995):** Quantification of recruitable coronary collateral blood flow in conscious humans and its potential to predict future ischemic events. J Am Coll Cardiol., 25 (7):1522–8.
11. **Caymaz O, Fak A, Tezcan H *et al.* (2000):** Correlation of myocardial fractional flow reserve with thallium-201 SPECT imaging in intermediate-severity coronary artery lesions. J Invasive Cardiol., 12 (7):345–50.
12. **Elfaramawy A, Hassan M, Nagy M *et al.* (2018):** Impact of fractional flow reserve on decision making in daily clinical practice: A single center experience in Egypt. The Egyptian Heart Journal, 70930: 161-165.
13. **Pijls N, van Schaardenburgh P, Manoharan G *et al.* (2007):** Percutaneous coronary intervention of functionally nonsignificant stenosis: 5-year follow-up of the DEFER Study. J Am Coll Cardiol., 49 (21):2105–11.
14. **McGeoch R, Oldroyd K (2008):** Pharmacological options for inducing maximal hyperaemia during studies of coronary physiology. Catheter Cardiovasc Interv., 71 (2):198–204.
15. **Leesar M, Abdul-Baki T, Akkus N *et al.* (2003):** Use of fractional flow reserve versus stress perfusion scintigraphy after unstable angina. Effect on duration of hospitalization, cost, procedural characteristics, and clinical outcome. J Am Coll Cardiol., 41(7):1115–21.
16. **Lopez-Palop R, Pinar E, Lozano I *et al.* (2002):** Clinical utilization of the coronary pressure wire. Rev Esp Cardiol., 55(3):251–7.
17. **Hacker M, Rieber J, Schmid R *et al.* (2005):** Comparison of Tc-99m sestamibi SPECT with fractional flow reserve in patients with intermediate coronary artery stenoses. J Nucl Cardiol., 12 (6):645–54.
18. **Bartunek J, Van Schuerbeeck E, De Bruyne B (1997):** Comparison of exercise electrocardiography and dobutamine echocardiography with invasively assessed myocardial fractional flow reserve in evaluation of severity of coronary arterial narrowing. Am J Cardiol., 79 (4):478–81.
19. **Courtis J, Rodes-Cabau J, Larose E *et al.* (2009):** Usefulness of coronary fractional flow reserve measurements in guiding clinical decisions in intermediate or equivocal left main coronary stenoses. Am J Cardiol., 103(7):943–9.