Original Article

Fractional Flow Reserve and Appropriateness of Angioplasty in Moderate Coronary Stenosis

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Abstract

Percutaneous coronary angioplasty (PTCA) of a coronary stenosis without documented ischemia at noninvasive stress testing is often performed, but its benefit is unproven. Coronary pressure– derived fractional flow reserve (FFR) is an invasive index of stenosis severity defined as the ratio of maximal blood pressure in a stenotic vessel to the normal maximal pressure in the same vessel. FFR is a reliable substitute for noninvasive stress testing and values below 75% identifies stenoses with hemodynamic significance. It is a method that can provide a reliable assessment of coronary stenosis especially in those with intermediate lesions. It can highly impact on decision-making in therapeutic planning and prevent many unnecessary procedures that are routinely done in these cases. In the present study, we report the results of FFR measurements in a series of patients, and this is the first report on the FFR measurement in Iran. The FFR measurement was performed for eleven vessels with intermediate stenosis, and in seven lesions (63.6%) it led to changes in the treatment strategy. On the basis of FFR, percutaneous coronary intervention (PCI) was changed into medical follow-up in five lesions, medical follow-up changed to PCI in one lesion, and coronary artery bypass grafting (CABG) changed to medical follow-up in another.

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Introduction

In patients with chest pain and a coronary stenosis at angiography, revascularization is warranted if objective evidence of reversible ischemia is present and medical therapy fails.[1] Yet, percutaneous coronary angioplasty (PTCA) is often recommended solely on the basis of the angiogram, although noninvasive testing for reversible ischemia is either negative, equivocal, or not performed at all.[2] In such patients, it is unclear whether the chest pain must be attributed to the coronary stenosis and whether PTCA improves event-free survival or functional class.[3] Fractional flow reserve (FFR) is an invasive index of the functional severity of a stenosis determined from coronary pressure measurement during cardiac catheterization.

FFR expresses maximum achievable blood flow to the

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myocardium supplied by a stenotic artery as a fraction of normal maximum flow. Its normal value is 1.0, and a value of 0.75 reliably identifies stenoses associated with inducible ischemia. The diagnostic accuracy of FFR for that purpose is 90%, which is higher than for any other invasive or noninvasive test.[3-7]

Retrospective studies suggest that the deferral of angioplasty in patients with FFR>0.75 is safe and results in an excellent clinical outcome.[6,8]

It is also suggested that the FFR measurement is helpful in decision-making in choosing an interventional procedure in coronary lesions of intermediate severity.[9,10] It is well shown that a high FFR rate after a procedure is accompanied by a good prognosis.[11,12] Furthermore, considering the growing numbers of patients with acute coronary syndromes undergoing catheterization without prior noninvasive imaging and the increasing numbers of patients with angiographic multivessel coronary artery disease, a complementary physiologic lesion assessment for direct revascularization is greatly helpful. FFR has, therefore, emerged as a simple, reliable, and reproducible physiologic index of lesion severity especially in multivessel coronary artery disease.[13-15] In this study, we report the results of FFR measurements in a series of patients with coronary artery disease and intermediate lesions that were referred to Tehran Heart Center. Our primary aim was to show the role of the FFR measurement in the therapeutic decision-making.

Methods

We performed a case series study in which the included patients were men with coronary artery disease and the following criteria: chest pain, angiographically detectable stenosis of moderate severity (defined as 50-70% diameter stenosis by visual examination) in one or more coronary arteries, uncertainty about whether the chest pain was related to reversible ischemia caused by the stenosis, and age between 45 and 75 years old.

All the patients underwent coronary artery angiography from the femoral approach by utilizing standard catheters and conventional views. Using angiographic results and other clinical and paraclinical findings, two other cardiologists made a diagnosis of moderate stenosis of a major coronary artery separately, and suggested a therapeutic plan. Then FFR studies were performed for studied coronary arteries by other physicians, and the results were compared with one another. We followed our patients clinically for 12 months (1-6-12 months).

Fractional flow reserve measurements were performed by using a standard end hole 6-7 F guiding catheter. A 0.014-inch guidewire with a mounted pressure sensor (pressure wire TM, V.4, RADI Medical System, Upsala, Sweden) was set at zero and placed distal to the stenosis to be measured. To induce maximal hyperemic vascular response, 50-80 µg and 30-50 µg of adenosine, as a vasodilator of vessels, were injected into the left coronary artery (LCA) and right coronary artery (RCA), respectively. Aortic pressure was measured using the guiding catheter. Fractional flow reserve was calculated as FFR = Pd/Pa, where Pd stands for mean post stenotic distal coronary pressure and Pa for mean proximal coronary pressure, which were both recorded simultaneously during maximal coronary hyperemia. FFR<0.75 was considered as an inducible ischemia. The selection of 0.75 as the cutoff value of FFR was based on previous studies.[16]

Results

The characteristics and risk factors of the included patients are depicted in Table 1. All the procedures were performed successfully without encountering any complications. No adverse effects were observed that were due to the pharmacological hyperemia. Table 2 depicts the results of angiographic and physiologic assessments of coronary arteries. It also summarizes consecutive therapeutic recommendations based on different methods.

Table 1. Patients' characteristics

Case No	Age (yr)	Sex	Chief Complaint	Risk Factor	Hx of MI	EF (%)	SPECT	No of Diseased Vessel*
1	49	Male	TCP	HLP, FH, C/S	No	60	Normal	1
2	68	Male	TCP	HLP	No	60	Inferolateral Ischemia	1
3	45	Male	TCP	C/S	No	65	Normal	1
4	60	Male	DOE	HLP, HTN, DM, FH	No	60	Normal	2
5	74	Male	TCP	No	Yes	60	Inferolateral Ischemia	2
6	48	Male	TCP	HLP, HTN	No	71	No	1
7	51	Male	ACP	HLP, HTN, C/S	Yes	60	Normal	1
8	51	Male	DOE	HLP, HTN, FH	Yes	60	No	1
9	49	Male	TCP	C/S	No	75	Normal	1

*Stenosis greater than 50%

Hx, History; MI, Myocardial infarction; EF, Ejection fraction; TCP, Typical chest pain; DOE, exertional dyspnea; ACP, Atypical chest pain; HLP, Hyperlipidemia; FH, Family history; C/S, Cigarette smoking; DM, Diabetes mellitus; HTN, Hypertension

Table 2. Angiographic results and physiologic assessments

C	1st Blind Reader Results			2nd Blind Reader Results			FFR Results			Post FFR Rec	Change in Strategy
	V	ST	Rec	V	ST	Rec	V	Rest	Hyp		
1	LAD	80	PCI	LAD	80	PCI	LAD	0.89	0.60	PCI	No
2	LAD	70	MFU	LAD	60	MFU	LAD	0.85	0.74	PCI	Yes
3	LAD	70	PCI	LAD	70	PCI	LAD	0.91	0.84	MFU	Yes
4	LAD	65	PCI	LAD	60	PCI	LAD	0.93	0.85	MFU	Yes
	RCA	60	MFU	RCA	50	MFU	RCA	1	0.95	MFU	No
5	LAD	70	PCI	LAD	75	PCI	LAD	0.96	0.88	MFU	Yes
	RCA	50	MFU	RCA	60	PCI	RCA	0.96	0.92	MFU	Yes
6	LAD	70	CABG	LAD	60	CABG	LAD	0.91	0.78	MFU	Yes
7	LCX	60	PCI	LCX	50	PCI	LCX	0.94	0.89	MFU	Yes
8	LAD	50	MFU	LAD	60	MFU	LAD	0.95	0.87	MFU	No
9	LAD	60	MFU	LAD	60	MFU	LAD	0.96	0.85	MFU	No

FFR, Fractional flow reserve; Rec, Recommendation; C, Case number; V, Vessel; ST, Stenosis percentage; Hyp, Hyperemic; LAD, Left anterior descending; RCA, Right coronary artery; LCX, Left circumflex artery; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting; MFU, Medical follow-up

Totally, the FFR measurement was performed for eleven vessels with intermediate stenosis, where in seven vessels (63.6%) it led to changes in the strategy of treatment. Of these seven vessels, PCI (based on initial recommendation by two blind readers) was changed into medical follow-up in five vessels. In the remaining vessels, our plan changed from CABG to medical follow-up in one vessel, and medical follow-up to PCI in another one. No adverse effects (concerning death or myocardial infarction) were observed during 12 months' follow-up.

Here we present two of our patients in whom the FFR measurement led to a revision in the strategic plan.

Case A

A 48-year-old man (the 2nd case in table 1) with a history of chest pain (function class=2) was referred to our center. He had an ejection fraction of 60% on a previous echocardiography. Angiographic assessment showed an eccentric borderline lesion at the proximal portion of the left anterior descending artery (Figure 1).

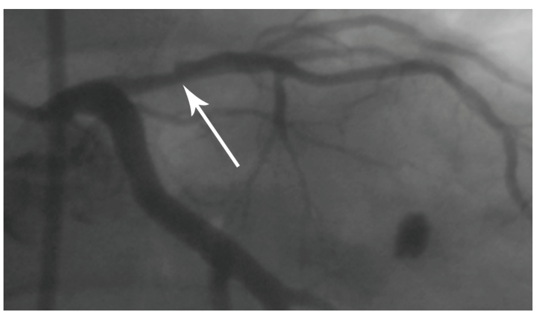
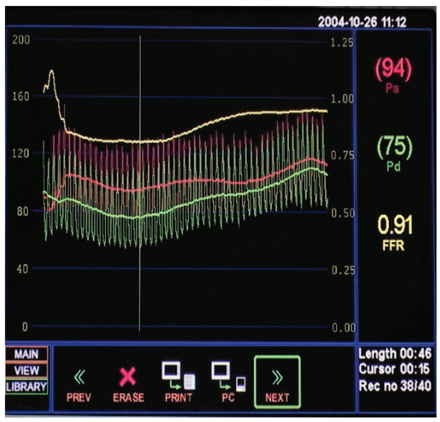
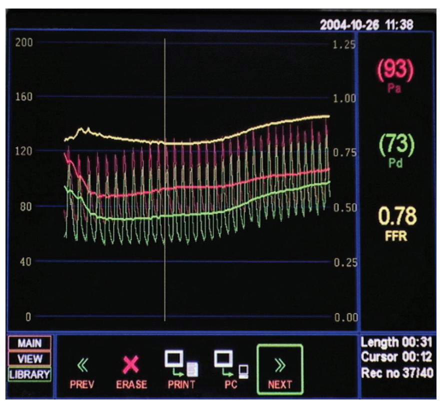


Figure 1. Eccentric lesion at left anterior descending artery in case A

CABG was recommended initially by both blind readers, but performing the FFR measurement led to changes in the treatment strategy about him.



(A)



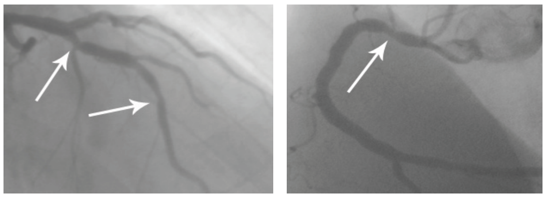
(B)

Figure 2. Rest (A) and hyperemic (B) Fractional Flow Reserve measurement in case A

As is shown in figure 2, the rest FFR of LAD was 0.91, whereas hyperemic FFR was 0.78. According to these data, post-FFR recommendation was a medical follow-up. In the next 12 months of follow-up, our patient remained symptom free.

Case B

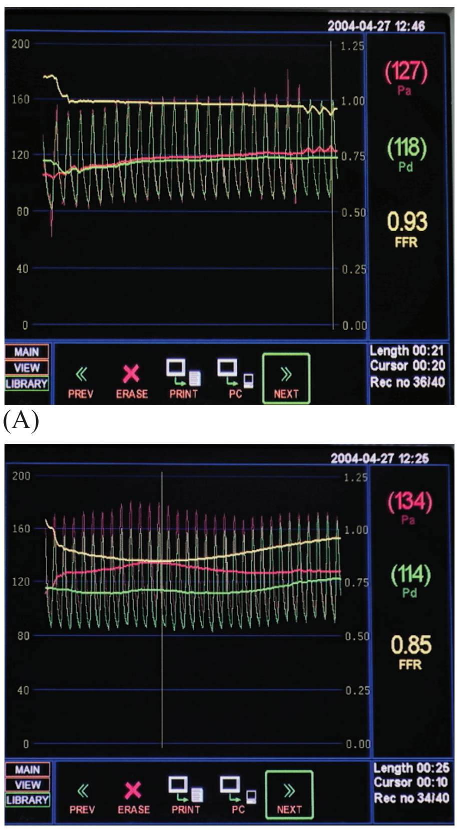
A 60-year-old man (the 4th case in table 1) with a history of dyspnea on exertion was referred to our center. He had an ejection fraction of 60% on a previously performed echocardiography. Following angiographic assessment, his initial diagnosis was a 2-vessel disease with a significant LAD lesion and a borderline RCA one. The initial recommendation was to perform a PCI for LAD and medical follow-up for RCA. The culprit lesions are shown in Figure 3.



(A) (B)

Figure 3. Angiographic findings in case B (arrows show stenosis), (A) Left anterior descending artery, (B) Right coronary artery

The FFR measurement was performed for LAD at rest and under hyperemic situation. As is shown in Figure 4, the rest FFR of LAD was 0.93, whereas hyperemic FFR was 0.85. According to these data, post-FFR recommendation was a medical follow-up. On 6 months' follow-up, the patient was symptom free.



(A)

(B)

Figure 4. Rest (A) and hyperemic (B) Fractional Flow Reserve results in case B

Discussion

It is now well documented that in some cases an angiographic assessment of coronary lesions are no more reliable for therapeutic decision-makings. This is particularly challenging in the cases of lesions with intermediate severity, defined as a percentage diameter stenosis between 50%-70%.[17,18] Even quantitative angiography has not been shown efficacious.19 Both techniques provide a two dimensional planar silhouette of the arterial lumen and, therefore, have limited accuracy in the setting of vessel tortousity or overlaps, bifurcational or eccentric lesions, diffusedly diseased arteries and vessels less than 2 mm in diameter. Furthermore, there is intraobserver as well as interobserver variability in the angiographic assessment of a coronary lesion.[17,19]

Performing myocardial perfusion scan along with angiography has facilitated clinical decision-making in so many cases, but limitations still remain. Some studies have shown that myocardial perfusion scan has limitations in cases of multiple vessel disease.[17] It is also incapable of depicting the culprit lesion in a single vessel with multiple stenoses.[20]

Recently, high-resolution cross-sectional imaging of arterial walls and lumen provided by intravascular ultrasonography (IVUS) has been considered highly accurate and can overcome limitations of conventional methods, as was mentioned above. By real – time visualization of vessel walls, an accurate assessment of the lumen size, plaque area, and internal composition can be possible.[21]

Fractional flow reserve is defined as the ratio of maximal blood pressure in a stenotic vessel to the normal maximal pressure in the same vessel, so that its measurement provides a physiologic assessment of coronary lesions.[22,23] The normal value of FFR is 1.0 in any patient and in any vessel. It is shown that a value of 0.75 reliably indicates inducible ischemia by a specific moderate coronary lesion with a sensitivity of 89% and specificity of 100%.[16] This index is highly reproducible and is not dependant on hemodynamic variations such as systemic blood pressure, heart rate, and contractility.[24] Its safety and feasibility were also noticed in our study.

A similar cut point was also evaluated for IVUS indexes such as minimum luminal diameter (MLD) and minimum luminal area (MLA). In a recent study directed by Jasti et al.[25], it was suggested that these parameters were correlated strongly with those of FFR and were, therefore, physiologically valid.

However, an analysis of IVUS data requires a higher degree of expertise and IVUS is more expensive to perform than FFR. Moreover, FFR can be used easily to investigate other arteries and to make pull back curves along the arteries with a high resolution to detect the source of ischemia in more complex patients.

Our cases consisted of patients with at least one intermediate stenosis in coronary arteries, as defined by primary angiography. All the patients were symptomatic at the time of referral, hence the tendency to recommend PCI on angiographic assessments. By performing the FFR measurement, we changed our therapeutic plan from PCI to medical follow-up in 5 vessels (45.5%) and from medical treatment to PCI in only one vessel (9.1%); in another case, the plan changed from CABG to medical treatment. Nonetheless, in four vessels (36.5%), the FFR measurement did not change our therapeutic plan. These results, like the ones in some other studies,[26] show that treatment recommendations based solely on angiographic results are not reliable and can lead to unnecessary procedures. We did not consider any adverse effects due to deferral of PCI in one year's follow-up.[27]

Conclusion

In summery, we conclude that FFR is to be considered as a safe measurement modality index in therapeutic decision-making especially in cases with borderline coronary lesions and prevents improper procedures in those patients. This study was designed in the setting of case series and it was relatively small in the numbers of patients. To have a better conclusion, further studies with a larger population should be carried out.

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